A budget optimization analysis for the treatment and potential elimination of hepatitis C virus infection in the United States

SAT-295

Olivier Ethgen[1,2], Yuri Sanchez Gonzalez[3], Jordan J. Feld[4]

[1]SERFAN innovation, Namur, Belgium; [2]University of Liège, Liège, Belgium; [3]AbbVie Inc., North Chicago, IL, USA; [4]Toronto Centre for Liver Disease, Toronto, ON, Canada

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

- Despite a growing body of evidence on the cost effectiveness of novel hepatitis C virus (HCV) treatments[1,2], there is a need to: (i) assist healthcare payers in the identification of the best strategy that optimizes the use of their available budgets for HCV treatment, and (ii) inform whether these investments can break even in a foreseeable future and secure a path towards HCV elimination
- As the total budget allocated to treat HCV in the United States (US) is expected to fall,[3] it is important to inform optimal treatment policies to substantiate the public health value of investments in HCV treatment

OBJECTIVES

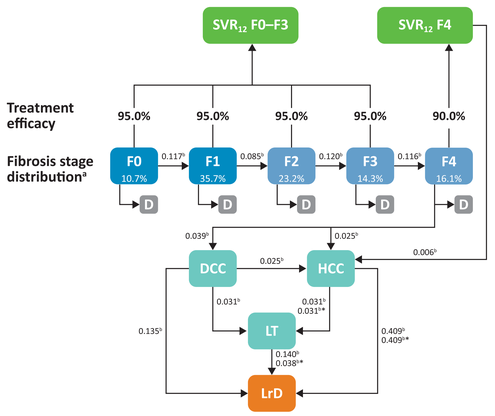
- To identify optimal therapeutic strategies on the basis of most favorable patient outcomes, subject to specified budget constraint and HCV epidemiology
- To assess whether up-front investments in HCV treatment could be recouped by society with future lower medical spending and improved quality-adjusted survival, and identify the potential time to break even

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 US diagnosed HCV population from 2017 until 2030
- The model used annual cycles for the eligible HCV population diagnosed across the five Metavir 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; SVR_{12}, sustained virologic response 12 weeks after treatment.

Table 1. Treatment Strategies

Strategies	Fibrosis Stages F0	F1	F2	F3	F4	Description
Strategy 1						No treatment at all
Strategy 2	•					Treat F0 only
Strategy 3	•	•				Treat F0-F1 only
Strategy 4	•	•	•			Treat F0-F1-F2 only
Strategy 5	•	•	•	•		Treat F0-F1-F2-F3 only
Strategy 6	•	•	•	•	•	Treat F0-F1-F2-F3-F4
Strategy 7		•	•	•	•	Treat F1-F2-F3-F4 only
Strategy 8			•	•	•	Treat F2-F3-F4 only
Strategy 9				•	•	Treat F3-F4 only
Strategy 10					•	Treat F4 only
Strategy 11	•	•	•	•	•	Treat F0-F1-F2-F3-F4 sequentially
Strategy 12	•	•	•	•	•	Treat F4-F3-F2-F1-F0 sequentially

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)

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 2**
- Cost inputs were obtained from published literature and included treatment costs, healthcare expenditures attributable to liver-related complications (including decompensated cirrhosis [DCC], hepatocellular carcinoma [HCC], liver transplant [LT] and liver-related death [LrD]) and extrahepatic manifestations (EHMs) associated with HCV infection (**Table 2**)

Table 2. Data Inputs

Data Input	Base
Prevalence 2017	
Prevalent cases in 2017[a]	3,500,000
Fraction diagnosed[b]	50%
Average age (years)[c]	50
Annual incidence	
Annual incident cases[d]	20,000
Fraction diagnosed[b]	50%
Average age (years)[c]	50
Health state utilities[e]	
SVR F0–F3	0.930
SVR F4[f]	0.827
F0	0.860
F1	0.860
F2	0.860
F3	0.830
F4 (CC)	0.810
DCC	0.700
HCC	0.670
LT*	0.780

Data Input	Base
Costs	
Treatment[c]	$80,000
Medical (annual costs)	
SVR F0–F3[e]	$225
SVR F4[e]	$225
F0 / F1 / F2 / F3[e]	$753
F4 (CC)[e]	$1,433
DCC[g]	$33,314
HCC 1st year[e]	$40,663
HCC sub. year[e]	$40,663
LT 1st year[e]	$190,301
LT sub. year[e]	$34,369
LrD[h]	$25,000
EHMs[i]	$12,000

*Refers to "prior to transplant" health state. Sources and assumptions: [a]Edlin BR, et al. *Hepatology*. 2015;62(5):1353-63. [b]Yehia BR, et al. *PLoS One*. 2014; 9(7): e101554.[c]Assumption. [d]Hepatitis C Online - HCV Epidemiology in the US http://www.hepatitisc.uw.edu/pdf/screening-diagnosis/epidemiology-us/core-concept/all. [e]Rein DB, et al. *Clin Infect Dis*. 2015; 15;61(2):157-68. [f]Multiplier from Leidner AJ, et al. *Hepatology*. 2015;61(6):1860-9. [g]McAdam-Marx C, et al. *J Manag Care Pharm*. 2011;17:531-46. [h]Dieguez et al. AASLD Oral Presentation 2016. [i]Reau et al. 2017 (AbbVie data on file H17.DOF.06). 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.

- Drug costs were computed based on the list price of all-oral direct-acting antiviral therapies and averaged at $80,000 per treatment course
- Quality-adjusted life years (QALYs) were estimated based on utility weights used in previous US-based health economic and public health assessments[4,5]
- Patient outcomes and costs were discounted at 3%

OUTCOMES

- Health outcomes included the projected number of QALYs, patients treated and patients reaching sustained virologic response (SVR), end-stage liver disease (ie, DCC, HCC or LT) or LrD
- Economic outcomes included HCV treatment costs, medical (liver-related and extrahepatic) costs and the value of improved patient outcomes (estimated at $100,000 per QALY gained[6])
- Time to break even was measured as the number of years required for up-front investments in HCV treatment to be fully recovered with the value of QALYs gained and/or with reduced medical costs in the future

ANALYSES

- First, we assessed the optimal treatment strategy that achieved the best possible liver outcomes (ie, highest number of SVRs and QALYs and lowest number of DCC, HCC, LT and LrD cases)
  - The annual treatment budget was assumed to decline by 5% per year from $10 billion in 2017 to $5.1 billion in 2030
- Second, we assessed the path to HCV elimination with the optimal treatment strategy under two budget expansion scenarios:
  - Annual treatment budget of $10 billion maintained throughout 2017–2030 (ie, no annual budget decline)
  - Annual treatment budget increased to $15 billion and maintained throughout 2017–2030
- Finally, we assessed the time to break even for an up-front investment to treat all fibrosis stages in 2017, relative to the optimal treatment strategy based on a $15 billion annual budget throughout 2017–2030. We considered this analysis from two healthcare perspectives:
  - Payer perspective valuing improved patient outcomes at $0 per QALY
  - Social perspective valuing improved patient outcomes at $100,000 per QALY

RESULTS

OPTIMAL TREATMENT: STEPWISE TREATMENT F4→F0 (STRATEGY 12)

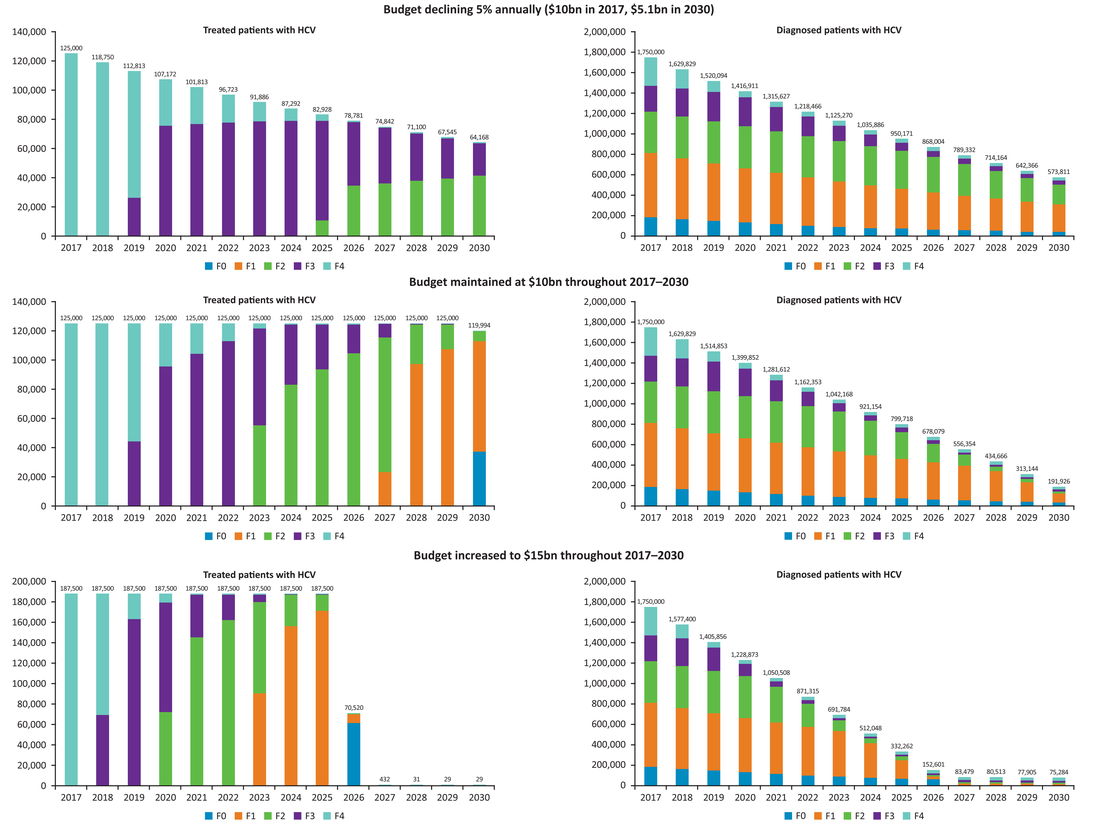
- Among all budget-feasible treatment options, the stepwise strategy to sequentially treat all fibrosis stages prioritizing the most advances cases (F4→F0) maximized favorable liver outcomes and minimized adverse liver outcomes by 2030 (**Table 3**)
- In contrast, the next best strategy of restricting treatment to stages F3–F4 yielded 219,054 fewer SVR cases, 65,734 fewer QALYs and an increase of 12,150 DCC, 4,621 HCC, 2,092 LT and 12,801 LrD cases

Table 3. Impact of Budget Expansion With the Optimal Treatment Strategy

Budget	SVR, n	DCC, n	HCC, n	LT, n	LrD, n	QALYs, n	Treatment Costs, bn	Liver-related Costs, bn	EHMs Costs, bn	Total Costs, bn
Budget declining 5% annually	1,126,729	23,663	39,684	5,041	43,645	14,059,756	$87.2	$19.6	$163.1	$269.9
Fixed $10 bn budget	1,513,328	23,057	38,219	4,908	42,407	14,156,993	$116.1	$18.7	$146.3	$281.1
Fixed $15 bn budget	1,643,655	18,176	32,836	3,915	34,941	14,345,307	$124.6	$15.5	$109.7	$249.8

bn, billion; DCC, decompensated cirrhosis; EHMs, extrahepatic manifestations; HCC, hepatocellular carcinoma; liver-related death (ie, death from DCC, HCC, and LT), LrD; LT, liver transplant; QALYs, quality-adjusted life years; SVR, sustained virologic response. Outcomes measured over 2017–2030.

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



bn=billion; F=Metavir fibrosis score; HCV=hepatitis C virus.

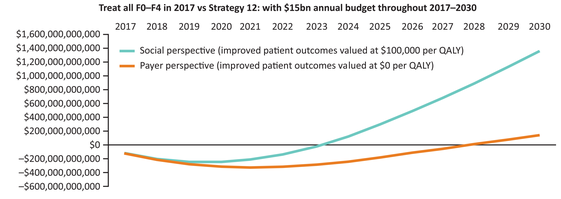
BENEFITS OF BUDGET EXPANSION UNDER THE OPTIMAL STEPWISE STRATEGY F4→F0 (FIGURE 2)

- Sustaining the HCV treatment budget at $10 billion throughout 2017–2030 improved population health outcomes and accelerated the path towards disease elimination compared with a declining budget
- An increased and sustained treatment budget of $15 billion throughout 2017–2030 achieved the best population health outcomes and lowest total cost since the greater up-front investments in treatment were fully offset by future savings in medical and EHMs costs (**Table 3**)

BREAK-EVEN ANALYSIS FOR INVESTMENTS TO TREAT ALL FIBROSIS STAGES IMMEDIATELY (FIGURE 3)

- From a payer's perspective, an up-front investment to treat all fibrosis stages in 2017 would cost $140 billion but break even by 2028 and generate a net surplus of $137 billion by 2030
- From a social perspective that values each QALY gained at $100,000, this $140 billion up-front investment would break even by 2023 and generate a net surplus of $1.35 trillion by 2030

Figure 3. Break-even Analysis



bn=billion; F=Metavir fibrosis score; HCV=hepatitis C virus; QALY=quality-adusted life year.

DISCUSSION

- As the sequential treatment of all fibrosis stages prioritizing most advances cases achieves the most favorable patient outcomes, treatment restrictions by fibrosis stage yields a suboptimal number of SVR cases, QALYs and adverse liver events
- If the current declining budget trends continue, our model suggests that there would be more than 0.5 million diagnosed HCV cases in 2030
- HCV treatment budgets should therefore be increased and sustained if the World Health Organization goal to cure ≥80% of HCV cases by 2030[7] is to be met
- Increased investment to treat HCV can be cost-saving. Treating all fibrosis stages immediately would yield a positive return to payers within 11 years, and to society within 6 years. While this effort would require an up-front investment of $140 billion, the net economic benefits to society could exceed $1 trillion by 2030

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, allowing for price erosion would further accelerate the path to HCV elimination and time to break even
- The model only focused on the diagnosed HCV population. Further analyses are needed to identify the optimal policies for the undiagnosed population regarding HCV screening, testing and linkage to care

CONCLUSIONS

- With increased and sustained levels of investment, the sequential treatment of all fibrosis stages prioritizing the most advanced cases provides the highest health benefits and fastest path to HCV elimination in the US
- Increased efforts to treat all patients diagnosed with HCV immediately could financially break even in 6–11 years and provide significant net economic benefits to payers and society thereafter

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. **Conflicts of Interest: 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. **Jordan Feld** has received consulting fees from AbbVie Inc., Gilead, Janssen and Merck, and research support from AbbVie Inc., Gilead, Janssen, Merck and Regulus.

ACKNOWLEDGEMENT

Editorial support for poster development was provided by Tom Owen, PhD, of Fishawack Facilitate, and funded by AbbVie.

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The cumulative prevalence and incidence of extra-hepatic manifestations in patients with hepatitis C virus infection: real-world evidence from the United States

SAT-216

Nancy Reau[1], Francis Vekeman[2], Eric Wu[2], Yanjun Bao[3], Yuri Sanchez Gonzalez[3]

[1]Rush University Medical Center, Chicago, IL; [2]Analysis Group, Inc., Boston, MA; [3]AbbVie Inc., North Chicago, IL, USA

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

- Between 2.7 and 3.9 million people are currently living with chronic hepatitis C virus (HCV) infection in the United States (US)[1]
- Previous studies have shown that HCV infection is associated with both hepatic complications (eg, cirrhosis, liver failure) and extra-hepatic manifestations ([EHMs] eg, chronic kidney disease [CKD], cardiovascular disease)[2-5]
- No previous study has assessed how the prevalence of a comprehensive list of potential EHMs changes over time and compared such differences between patients with HCV vs those without

OBJECTIVE

- To compare the 5-year cumulative prevalence and incidence of EHMs among patients with and without HCV in the US

METHODS

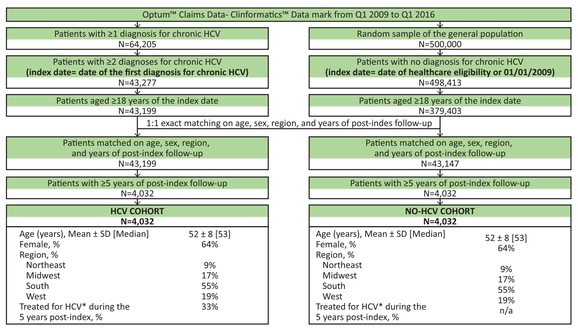
DATA SOURCE

- Optum™ Claims Data - Clinformatics™ Data Mart (01/01/2009 – 31/01/2016; US), a de-identified health claims dataset, including patients' medical, prescription drug, laboratory, and eligibility information
- Patients included: HCV cohort comprised of all adult patients with a diagnosis code for chronic HCV (International Classification of Disease, Ninth Revision [ICD-9] diagnosis codes 070.44 and 070.54; ICD-10 diagnosis code B18.2; N = 64,205); no-HCV cohort comprised of a random sample of the general adult population (N = 500,000) from which patients with diagnosis codes for chronic HCV were excluded

STUDY DESIGN AND STUDY COHORTS

- Retrospective analysis of the cumulative prevalence and incidence of EHMs using longitudinal claims data
- Two cohorts matched 1:1 on age, sex, region, and years of follow-up: HCV and no-HCV cohorts (exact match; see **Figure 1** for cohort selection and definition of index date)
- The index date was selected as the day of first HCV diagnosis for the HCV cohort and the first day of insurance eligibility for the no-HCV cohort

Figure 1. Selection of HCV and no-HCV study cohorts and demographic characteristics



*HCV treatment included: boceprevir, daclatasvir, dasabuvir, elbasvir, grazoprevir, interferons alpha, ledipasvir, ombitasvir, paritaprevir, ribarvin, ritonavir, simeprevir, sofosbuvir, telaprevir

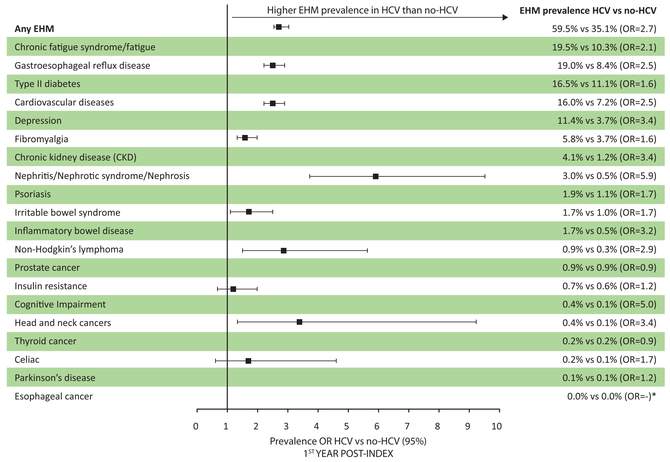
OUTCOMES AND STATISTICAL ANALYSES

- Twenty EHMs were investigated based on a global literature review[6] (**Figure 2**)
- To assess the evolution of EHM risks over time, EHM prevalence, defined as the proportion of patients living with a given EHM at a given point in time, was measured for each of the 20 EHMs in the 1st and 5th year post-index
- Cumulative incident cases (ie, newly diagnosed) from the 2nd to 5th year post-index were also reported
- Prevalence odds ratios (ORs) were estimated from unadjusted conditional logistic regression models that account for matching; incidence ORs were estimated from logistic regression models adjusted for the age, sex, and region (matching did not hold in the subgroup of patients at risk after the 1st year post-index)

RESULTS

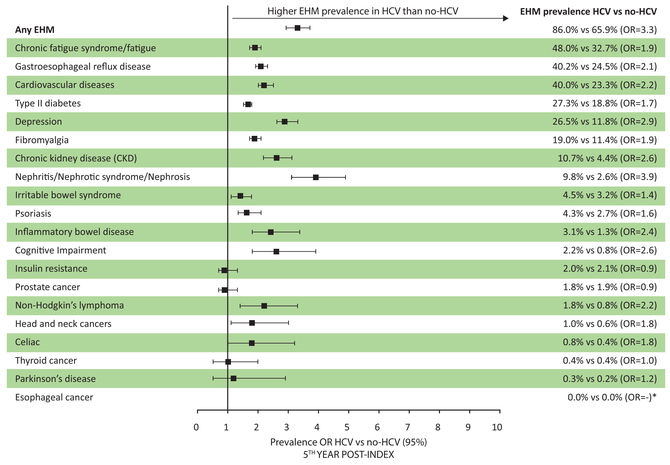
- The prevalence of any EHM in the 1st year post-index date was 60% in the HCV cohort and 35% in the no-HCV cohort (prevalence OR: 2.7; **Figure 2**), and it increased by the 5th year to a cumulative prevalence of 86% and 66%, respectively (prevalence OR: 3.3; **Figure 3**); the 4-year incidence of any EHM was 65% and 48%, respectively (incidence OR: 2.1; **Figure 4**)
- Already in the 1st year post-index, the HCV cohort had a significantly higher prevalence of EHMs than the no-HCV cohort; this early difference is likely due to the fact that patients in the HCV cohort were infected before the diagnosis and had an increased risk of EHM prior to the index date
- A similar trend with higher prevalence in the HCV vs the no-HCV cohort was also observed for specific EHMs, including for conditions previously not recognized as EHMs such as inflammatory bowel disease and gastroesophageal reflux disease (prevalence OR in 5th year post-index: 2.4 and 2.1, respectively; **Figure 3**)

Figure 2. Prevalence of 20 EHMs among HCV vs no-HCV cohorts in the 1st year post-index (by order of frequency in HCV cohort)



*Prevalence OR could not be calculated (at 1st year post-index there were 2 patients with esophageal cancer in the HCV cohort vs none in the no-HCV cohort)

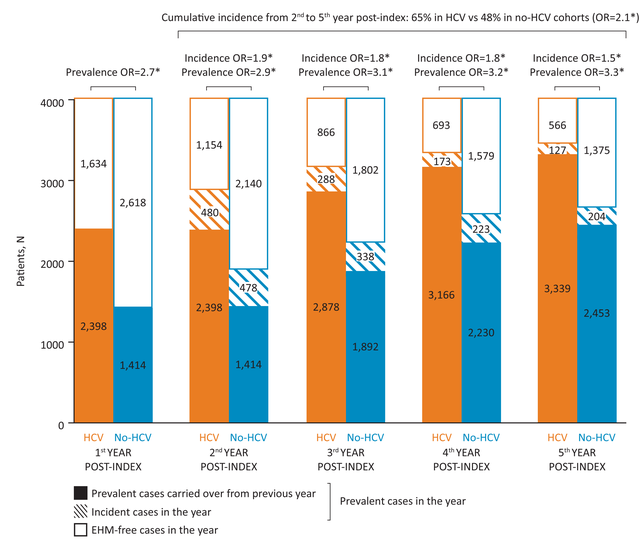
Figure 3. Prevalence of 20 EHMs among HCV versus no-HCV cohorts in the 5th year post-index (by order of frequency in HCV cohort)



*Prevalence OR could not be calculated (at 5th year post-index there were 3 patients with esophageal cancer in the HCV cohort vs none in the no-HCV cohort)

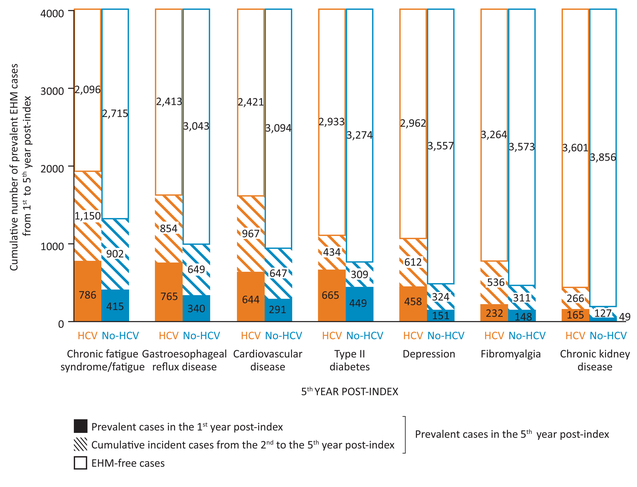
- Incident cases continued to accumulate from the 2nd to 5th year post-index even for EHMs that had very high prevalence in the 1st year post-index (**Figure 5**)
- Some severe and relatively uncommon conditions in the general population, such as CKD, reached a prevalence of >10% among the HCV population in the 5th year post-index (**Figure 5**)
- Some EHMs that are more characteristic of older populations (eg, cognitive impairment, Parkinson's disease, and cancer) had low prevalence in both study cohorts; this could be explained by the fact that the cohorts included relatively young patients (median age 53 years)

Figure 4. Cumulative prevalent and incident cases of any EHM from the 1st to the 5th year post-index



*p < 0.05

Figure 5. Prevalent and incident cases of selected* specific EHMs in the 5th year post-index



*EHMs with prevalence > 10% in at least one cohort in the 5th year post-index

DISCUSSION

- In light of the growing EHM risks associated with HCV infection, current restrictions on treatment access based on fibrosis stage may exacerbate the clinical burden to patients and economic burden to payers in both the short and long terms
- The gap in EHMs observed in patients with HCV as early as their year of diagnosis not only persists but increases over time compared with patients without HCV. This suggests a potential role for timely diagnosis, linkage to care, and early treatment to close this gap

LIMITATIONS

- The study sample comprised of commercially-insured patients may not be representative of the general HCV population
- Some patients included in the no-HCV cohort could be HCV-infected but not yet diagnosed, and thus the prevalence OR of EHMs could have been underestimated
- The HCV and no-HCV cohorts were matched on age, sex, region, and duration of follow-up; however, residual confounding due to other factors associated with HCV infection (eg, riskier behaviors in the HCV cohort) may persist
- This study was subject to the limitations of retrospective studies based on healthcare claims data, including occasional errors or claim omissions. However, such limitations would likely affect both HCV and no-HCV cohorts similarly
- The extent to which the excess EHM risk of HCV financially burdens the healthcare system or can be mitigated with effective HCV treatment remains an area of further research
- Further research is also needed on the best policies to close the existing EHM gaps between HCV and no-HCV patients, which may involve targeted HCV screening, adequate linkage to care, and treatment upon diagnosis regardless of fibrosis stage

CONCLUSIONS

- EHMs pose a high clinical burden on patients with HCV, which grows over time and could translate into a substantial economic burden
- Expanded HCV screening and early treatment may help reduce the risk of EHMs associated with HCV by closing the gap in EHM prevalence and delaying the incidence of EHMs
- The results of the current study may be particularly relevant to inform therapeutic and policy decisions related to HCV screening, linkage to care, and treatment upon diagnosis or at early fibrosis stages

DISCLOSURES

Funding for this research was provided by AbbVie Inc.; the study sponsor was involved in all stages of the study research and manuscript preparation. **Nancy Reau** is an employee of Rush University Medical Center and is a consultant for AbbVie Inc. She is also a consultant for Gilead Sciences, Inc., Merck and Co, Inc., and Bristol-Myers Squibb, and her institution has received research support from AbbVie Inc. and Gilead Sciences, Inc. **Eric Wu** is an employee of Analysis Group which received consultancy fees from AbbVie Inc. for conducting research analysis. **Francis Vekeman** was an employee of Analysis Group at the time this analysis was conducted. **Yanjun Bao** and **Yuri Sanchez Gonzalez** are employees of AbbVie Inc. and may own AbbVie stock or stock options.

ACKNOWLEDGEMENT

Raluca Ionescu-Ittu, Willy Wynant, and Hela Romdhani, employees of Analysis Group, Inc., contributed to the data analysis. AbbVie provided funding to Analysis Group for this work.

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Effect of hepatitis C treatment with ombitasvir/paritaprevir/ritonavir + dasabuvir regimen on patient's health-related quality of life: Analysis of Phase 3a and Phase 3b clinical trials

SAT-268

Sammy Saab[1], Darshan Mehta[2,3], Stacie Hudgens[4], Nathan Grunow[4], Yanjun Bao[3], Brett Pinsky[3]

[1]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA; [2]Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, USA; [3]Health Economics and Outcomes Research, AbbVie Inc., North Chicago, IL, USA; [4]Clinical Outcomes Solutions, Tucson, AZ, USA

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

- Chronic hepatitis C (CHC)-infected patients have diminished health-related quality of life (HRQoL),[1–4] particularly driven by fatigue[5–9]
- Patients treated with an interferon (IFN)- and ribavirin (RBV)-based regimen reported a significant decrease in their HRQoL prior to and during treatment[10]
- IFN- and RBV-free regimens comprising of a combination of direct acting antivirals (DAAs) have been approved by the FDA for certain genotypes (GT) of hepatitis C virus (HCV) patients. Prior patient-reported outcome (PRO) studies on these DAA regimens have demonstrated an improvement in HRQoL during the treatment period. This improvement was seen until 24 weeks post-treatment[11–13]
- Based on near 100% sustained viral response (SVR)12 rates observed in clinical trials, the ombitasvir/paritaprevir (identified by AbbVie and Enanta)/ritonavir + dasabuvir (3D) regimen was recently approved for use without RBV for GT1b patients with or without compensated cirrhosis[14]
- The impact of treatment with the 3D regimen for this specific HCV population is not well defined

OBJECTIVES

- This study aims to report on the impact of treatment with the 3D regimen on patient-reported function and quality of life as measured by the 36-Item Short Form Health Survey (SF-36) and the EuroQol five dimensions questionnaire (EQ-5D) and fatigue subscale (FS) for HCV GT1b patients during treatment and up to 52 weeks post-treatment

METHODS

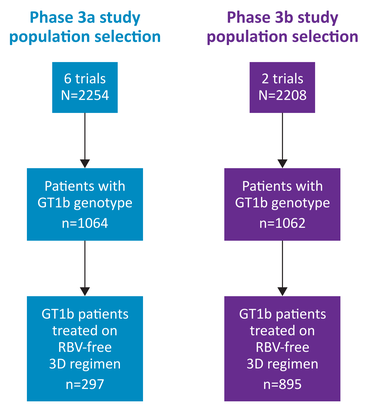
STUDY DESIGN

- The study pooled and analyzed PROs from:
  - Six registrational Phase 3a trials (Phase 3a study population)
    - SAPPHIRE I[15], SAPPHIRE II[16], PEARL II[17]/III/IV[18], TURQUOISE II[19]
    - PRO data collected: SF-36 and EQ-5D
  - Two Phase 3b trials (Phase 3b study population)
    - TOPAZ I (NCT02219490) and TOPAZ II (NCT02167945)
    - PRO data collected: SF-36 and FS of Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)
- Patient selection is described in **Figure 1**
- The study period comprised of the treatment period and 48 or 52 weeks of post-treatment follow-up for Phase 3a and 3b trials, respectively

PRO QUESTIONNAIRES

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

Figure 1. Patient Selection



Note: Six Phase 3a trials (Phase 3a study population): SAPPHIRE I[15], SAPPHIRE II[16], PEARL II[17]/III/IV[18], TURQUOISE II[19]. Two Phase 3b trials (Phase 3b study population): TOPAZ I (NCT02219490) and TOPAZ II (NCT02167945)

DATA ANALYSIS

Empirical Analysis: Mixed Models

- PRO scores at each time point were analyzed using linear mixed models independently for Phase 3a and Phase 3b study populations
- Models were adjusted for:
  - Fixed effects: Baseline PRO domain score, region, baseline viral load, treatment duration, treatment by time interaction, prior treatment history, baseline fibrosis stages, patient's age, and history of drug use
  - Random effects: Study enrollment
- The change from baseline was predicted based on the model coefficients and tested for statistical significance

Minimally Important Difference (MID) Changes: Proportional Analysis

- A comparative analysis of the proportion of the study populations achieving MID on PRO variables was performed at treatment week 4, post-treatment week 12, and the end of follow-up (post-treatment week 48/52)
- Based on prior published HCV-specific literature, clinically meaningful improvements were defined as increases of:
  - 2 points on SF-36 mental and physical component score[11]
  - 3 points on the SF-36 component domain score, except VT domain[11]
  - 4.2 points on VT domain[23]
  - 3 points on FS of FACIT-F[24]

Table 1. PRO Questionnaires

Measure	Description	Scoring
SF-36v2	• Total of 36 items targeting functional health and well-being[20] • The two major components and contributing domains are: – Physical component summary score: physical functioning (PF), role physical (RP), bodily pain (BP), and general health (GH) – Mental component summary score: vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH) • SF-36 VT domain has been regarded as the most comprehensive well-being measure for a patient who suffers from HCV[5,8,10]	• The total scores on each domain range from 0 to 100 • Higher scores indicate a better HRQoL
EQ-5D-5L	• Comprises of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each of which is rated on 5 levels of severity[21] – 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-5L range from 0 to 1 and on EQ-5D VAS range from 0 to 100 • Higher scores indicate a better HRQoL
FS	• This is a symptom-specific domain of the FACIT-F measuring fatigue in a variety of chronic diseases or health conditions[22]	• Total scores range from 0 to 52 • Higher FS scores indicate a lesser degree of fatigue

EQ-5D-5L=EuroQol five dimensions questionnaire with five-level scale; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; FS=fatigue subscale; HRQoL=health-related quality of life; SF-36=36-Item Short Form Health Survey; VT=vitality.

RESULTS

STUDY POPULATION

- A total of 297 GT1b patients and 895 GT1b patients from Phase 3a and Phase 3b trials, respectively, were included for analysis
- Baseline demographics of the study population are shown in **Table 2**

PHASE 3A STUDY POPULATION (TABLE 3)

Baseline HRQoL

- Baseline values of each instrument were equivalent to those in the general population

Treatment Period HRQoL

- Across domains and instruments, there were no statistical or clinically meaningful declines in patient HRQoL during the treatment period
- Patients began to report increases in HRQoL on mental health (MH) and general health (GH) domains of SF-36 and the health utility index of EQ-5D that were statistically significant by treatment week 4
- Increases observed during the treatment period persisted during the post-treatment period

Post-treatment HRQoL

- By post-treatment week 12, patients reported increases in HRQoL scores versus baseline for the SF-36 mental component score and its domains, and for EQ-5D. These increases from baseline were statistically significant
- By post-treatment week 48, there was a statistically significant increase across domains and instruments

Table 2. Demographics of Study Population

GT1b population: RBV-free therapy	Phase 3a study population (n=297)	Phase 3b study population (n=895)
Age, mean (SD); years	50.7 (11.8)	51.9 (12.6)
Female	160 (54.1%)	513 (57.3%)
Race		
White	274 (92.5%)	847 (94.6%)
Black	16 (5.4%)	28 (3.1%)
Asian	3 (1.1%)	18 (2.1%)
Others	2 (0.7%)	2 (0.2%)
Region		
Australia/New Zealand and others		615 (68.7%)
Europe	233 (78.5%)	141 (15.8%)
North America/USA	64 (21.6%)	139 (15.5%)
Prior diabetes history (yes)[a]	19 (6.4%)	42 (5.6%)
Fibrosis Stage		
F0–F1	200 (67.6%)	606 (67.7%)
F2	66 (22.3%)	136 (15.2%)
F3	30 (10.1%)	150 (16.8%)
F4	0	3 (0.3%)
Baseline HCV viral load ≥800,000 IU/mL	229 (77.0%)	567 (63.5%)
BMI ≥30 kg/m²[b]	62 (20.9%)	151 (16.9%)
Injection drug user (yes)	34 (11.5%)	
HOMA-IR ≥3[c]	70 (27.7%)	252 (31.6%)
Treatment naïve	209 (70.4%)	454 (50.7%)
P/R experienced	88 (29.6%)	441 (49.3%)

[a]Remaining percentage represents no diabetes; [b]remaining percentage represents <30 kg/m²; [c]remaining percentage represents <3. BMI=body mass index; HCV=hepatitis C virus; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; P/R=peginterferon/ribavirin.

Table 3. Longitudinal Mixed Model Results: Phase 3a

	Unadjusted baseline value (SE)	Average adjusted change from baseline at W4 (SE)	Average adjusted change from baseline at EOT (SE)	Average adjusted change from baseline at PTW12 (SE)	Average adjusted change from baseline at EOF (SE)
SF-36 MCS	50.47 (0.59)	0.40 (0.38)	0.14 (0.48)	1.67* (0.49)	2.39* (0.49)
SF-36 Vitality	55.16 (0.59)	−0.72 (0.40)	−0.5 (0.5)	2.06* (0.52)	2.84* (0.52)
SF-36 Social Functioning	50.71 (0.48)	−0.04 (0.38)	−0.29 (0.46)	1.24* (0.47)	1.92* (0.47)
SF-36 Mental Health	49.95 (0.61)	0.88* (0.41)	0.88 (0.49)	1.81* (0.51)	2.64* (0.51)
SF-36 Role Emotional	49.47 (0.56)	−0.09 (0.42)	−0.63 (0.49)	0.62 (0.50)	1.28* (0.50)
SF-36 PCS	51.97 (0.47)	−0.38 (0.29)	−0.09 (0.36)	0.64 (0.37)	1.42* (0.37)
SF-36 Physical Functioning	51.24 (0.49)	−0.45 (0.32)	−0.55 (0.36)	0.56 (0.36)	1.04* (0.36)
SF-36 Role Physical	50.49 (0.49)	−0.66 (0.36)	−0.70 (0.43)	0.83 (0.44)	1.32* (0.44)
SF-36 General Health	49.61 (0.58)	0.75* (0.34)	1.4* (0.42)	1.76* (0.44)	2.76* (0.44)
SF-36 Bodily Pain	53.49 (0.58)	0.12 (0.46)	0.35 (0.54)	0.47 (0.55)	1.84* (0.55)
EQ-5D HUI	0.88 (0.01)	0.01* (0.01)	0.01 (0.006)	0.02* (0.01)	0.03* (0.01)
EQ-5D VAS	82.24 (0.83)	0.87 (0.51)	2.35* (0.65)	4.20* (0.67)	5.46* (0.67)

*p<0.05. EOF=end of follow-up (48 weeks); EOT=end of treatment; HUI=health utility index; MCS=mental component summary score; PCS=physical component summary score; PTW=post-treatment week; SE=standard error; VAS=visual analogue scale; W=week. The table presents predicted change from baseline at selected time points from linear mixed models. The PRO scores at each time point were analyzed adjusting for baseline PRO domain score, region, baseline viral load, treatment duration, treatment by time interaction, prior treatment history, baseline fibrosis stage, patient's age, and history of drug use as fixed effects. Study enrollment was included as a random effect. Study coefficients were not significant, indicating no statistically significant variation between studies.

PHASE 3B STUDY POPULATION (TABLE 4)

Baseline HRQoL

- Baseline values across SF-36 domains and component scores were lower than those in the general population

Treatment Period HRQoL

- Across domains and instruments there was no statistical or clinically meaningful decline in patient HRQoL during the treatment period
- Patients from Phase 3b trials began to report an increase in HRQoL across all SF-36 domains by treatment week 4
- Increases observed during the treatment period persisted during the post-treatment period

Post-treatment HRQoL

- Patients reported improvements on the SF-36 component scores at post-treatment weeks 12 and 52 that were statistically significant and clinically meaningful

Table 4. Longitudinal Mixed Model Results: Phase 3b

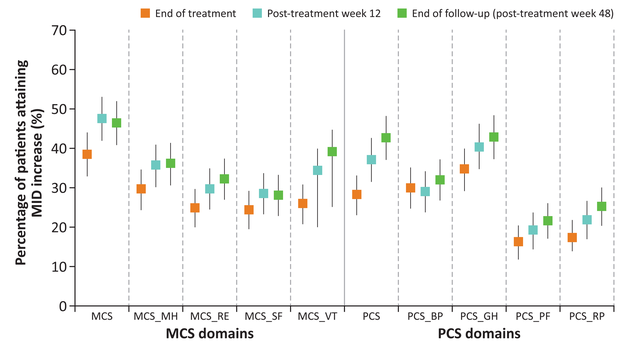
	Unadjusted baseline value (SE)	Average adjusted change from baseline at W4 (SE)	Average adjusted change from baseline at EOT (SE)	Average adjusted change from baseline at PTW12 (SE)	Average adjusted change from baseline at EOF (SE)
SF-36 MCS	47.19 (0.38)	1.76* (0.25)	2.08* (0.32)	3.53* (0.35)	3.37* (0.43)
SF-36 Vitality	51.27 (0.36)	1.62* (0.25)	2.76* (0.32)	4.82* (0.35)	4.71* (0.44)
SF-36 Social Functioning	47.50 (0.35)	1.67* (0.25)	1.95* (0.31)	2.87* (0.34)	2.71* (0.41)
SF-36 Mental Health	47.61 (0.37)	1.84* (0.26)	2.02* (0.32)	3.09* (0.35)	3.17* (0.43)
SF-36 Role Emotional	46.62 (0.38)	0.57* (0.28)	0.99* (0.34)	2.31* (0.37)	2.19* (0.45)
SF-36 PCS	50.08 (0.28)	0.58* (0.17)	1.47* (0.22)	2.18* (0.24)	2.16* (0.30)
SF-36 Physical Functioning	49.76 (0.29)	0.11 (0.18)	0.94* (0.23)	1.60* (0.25)	1.78* (0.31)
SF-36 Role Physical	47.92 (0.33)	0.30 (0.23)	0.86* (0.29)	2.18* (0.31)	2.31* (0.39)
SF-36 General Health	46.35 (0.33)	2.32* (0.20)	3.69* (0.26)	4.37* (0.29)	4.33* (0.36)
SF-36 Bodily Pain	51.82 (0.35)	1.08* (0.25)	1.37* (0.31)	2.00* (0.34)	1.68* (0.42)
FS	39.76 (0.35)	1.21* (0.23)	2.42* (0.28)	3.89* (0.32)	4.34* (0.39)

*p<0.05. EOF=end of follow-up (52 weeks); EOT=end of treatment; FS=fatigue subscale of FACIT-F; HUI=health utility index; MCS=mental component summary score; PCS=physical component summary score; PTW=post-treatment week; SE=standard error; VAS=visual analogue scale; W=week.
The table presents predicted change from baseline at selected time points from linear mixed models. The PRO scores at each time point were analyzed adjusting for baseline PRO domain score, region, baseline viral load, treatment duration, treatment by time interaction, prior treatment history, baseline fibrosis stage, patient's age, and history of drug use as fixed effects. Study enrollment was included as a random effect. Study coefficients were not significant, indicating no statistically significant variation between studies.

MID Increase

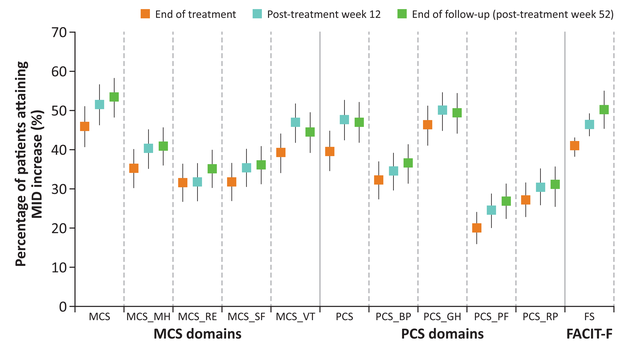
- MID increases are shown for Phase 3a and Phase 3b in **Figures 2** and **3**, respectively
- The percentage of patients experiencing clinically meaningful changes was sustained and improved during the post-treatment period

Figure 2. MID Increases: Phase 3a



Error bars denote 95% confidence intervals. BP=bodily pain; GH=general health; MCS=mental component summary score; MH=mental health; PCS=physical component summary score; PF=physical functioning; RE=role emotional; RP=role physical; SF=social functioning; VT=vitality.

Figure 3. MID Increases: Phase 3b



Error bars denote 95% confidence intervals. BP=bodily pain; FS=fatigue score; GH=general health; MCS=mental component summary score; MH=mental health; PCS=physical component summary score; PF=physical functioning; RE=role emotional; RP=role physical; SF=social functioning; VT=vitality.

DISCUSSION

- This study is the first comprehensive assessment of GT1b patient experience during and post-treatment with an RBV-free 3D regimen for CHC
- Patients enrolled in Phase 3b trials had a lower baseline PRO score compared with patients enrolled in Phase 3a trials. This may be one of the driving factors for Phase 3b trial patients demonstrating higher improvements at subsequent follow-up time points
- The GT1b population, treated with the RBV-free 3D regimen, did not report decrements in their HRQoL during the treatment period, which are commonly attributed with RBV
- Post-treatment, there were improvements in HRQoL that were both clinically and statistically significant. Domains with the largest improvements included the VT domain of SF-36 and FS in FACIT-F
- Our results are consistent with HRQoL gains documented with other IFN/RBV-free DAA regimens[11–13, 25]

STRENGTHS & LIMITATIONS

STRENGTHS

- PRO instruments used in this study have been validated and used widely across indications and geographies
- Results from these analyses were unique in terms of the length of follow-up data reported; PRO data were collected until 48 weeks post-treatment for Phase 3a trials and 52 weeks post-treatment for Phase 3b trials

LIMITATIONS

- The current study did not include GT1b cirrhotic patients from TURQUOISE III trial, since this study aimed to provide long-term HRQoL data for the study population. The TURQUOISE III trial collected data until 24 weeks post treatment
- 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
- Due to the multicenter nature of the clinical trials, bias might be incorporated due to site-specific peculiarities. Our mixed models controlled for study region to reduce this possibility

CONCLUSIONS

- This study demonstrates that treatment with RBV-free 3D regimen for HCV has a positive impact on HRQoL in GT1b patient populations that is maintained at follow-up of 48 and 52 weeks

DISCLOSURES

Design and study conduct for the study were approved 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. **Conflicts of Interest: Sammy Saab:** Consultant to and serves on speaker bureau for AbbVie, BMS, Gilead, Janssen, and Merck. **Darshan Mehta:** Financially supported for graduate research work by AbbVie as a part of a fellowship agreement between AbbVie and University of Southern California (USC). **Brett Pinsky and Yanjun Bao:** Employees of AbbVie Inc. and may own stocks and/or options of the company. **Nathan Grunow and Stacie Hudgens:** Employees of Clinical Outcomes Solutions hired by AbbVie Inc. to provide consulting services on this project.

ACKNOWLEDGEMENT

Editorial support for poster development was provided by Rebecca Wylie of Fishawack Facilitate and funded by AbbVie.

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abbvie

Early versus delayed hepatitis C treatment provides increased health benefits at lower costs: A UK cost-effectiveness analysis of genotypes 1 and 4 treatment-naïve patients

SAT-294

Yuri Sanchez Gonzalez[1], Andy Ingram[1], Claire Lindsay[1], Hélène Parisé[2], Suchin Virabhak[2]

[1]AbbVie Inc., North Chicago, IL, USA; [2]Medicus Economics, Boston, MA, USA

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

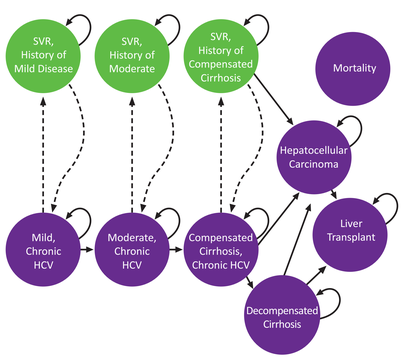
- An estimated 214,000 people in the United Kingdom (UK) are chronically infected with hepatitis C virus (HCV)[1]
- HCV disease progression can occur over a 20–50-year period;[2] long-term sequelae of chronic infection may include cirrhosis, liver decompensation, hepatocellular carcinoma (HCC), and liver transplantation (LT)[3,4]
- Patients in early-stage fibrosis may have limited access to highly effective treatment
- The costs of disease progression and complications, including decompensated cirrhosis (DCC), HCC, and LT, are major drivers of the economic burden of HCV[5]
- While achievement of SVR is associated with reduced risk of liver-related complications, patients who achieve SVR from more severe liver disease states have been shown to continue to face an excess risk of liver disease complications including HCC, LT, and liver-related mortality[6]
- Therefore, early treatment is believed to reduce the overall downstream medical costs compared with treatment in later disease stages[7–9]
- Recent studies have demonstrated the cost-effectiveness of the 3D regimen of ombitasvir/paritaprevir (identified by AbbVie and Enanta)/ritonavir and dasabuvir ± ribavirin (RBV) for treatment of genotype (GT) 1 patients, and the 2D regimen of ombitasvir/paritaprevir/ritonavir ± RBV for treatment of GT4 patients, vs previous and current standards of care[10,11]
- However, the cost effectiveness of treating patients in early- vs late-stage fibrosis with 3D or 2D is not well understood

OBJECTIVE

- To determine the lifetime risks of liver-related morbidity and mortality and the cost-effectiveness of receiving treatment with AbbVie 3D or 2D regimens ± RBV at different fibrosis stages in the UK

METHODS

Figure 1. Model Structure



Note: Health states are depicted by ellipses, while arrows represent permissible transitions between health states. Hashed arrows depict the possibility of achieving sustained virologic response (SVR). Dotted arrows depict a potential reinfection. Death is possible from any health state. Liver-related death is possible from decompensated cirrhosis, hepatocellular carcinoma, and liver transplant.

MODEL DESIGN

- A Markov model of the natural history of HCV was developed based on previous literature (**Figure 1**)[10,11]
- Target population included treatment-naïve GT1 patients treated with 3D ± RBV, and treatment-naïve GT4 patients treated with 2D ± RBV
- Comparative analyses were carried out for patients in different disease states by METAVIR fibrosis:
  - Mild (F0–F1)
  - Moderate (F2–F3)
  - Compensated cirrhosis (F4)
- The model was run over a lifetime horizon with patients entering the model at each disease state and receiving treatment with 3D or 2D ± RBV
- Patients with mild or moderate fibrosis who achieve SVR were assumed to be cured
- Patients with compensated cirrhosis were assumed to face an excess risk of HCC, even after achieving SVR, but did not progress to DCC
- For patients who achieve SVR, HCV reinfection was possible. Reinfected patients were assumed to transition back to their respective fibrosis state prior to achieving SVR and then progress through the more severe health states at the same rate as untreated patients
- Death from liver disease (LrD) could occur from the DCC, HCC, and LT states; death from non-liver causes could occur from any state
- Transition probabilities were derived from previously published cost-effectiveness studies (**Table 1**)

Table 1. Annual Transition Probabilities

	Base Probability
Fibrosis Progression, Mild/Moderate/CC[a]	
Mild to Moderate	0.025
Moderate to CC	0.037
Non-fibrosis Disease Progression	
Recovered, no HCV, History of Severe Fibrosis (CC) to HCC[b]	0.012
CC to DCC[c]	0.039
CC to HCC (First Year)[c]	0.014
DCC to HCC (First Year)[c]	0.014
Liver Transplant	
DCC to Liver Transplant (First Year)[d]	0.020
HCC to Liver Transplant (First Year)[e]	0.020
Liver-related Mortality	
DCC to Liver Death[c]	0.130
Liver Transplant to Liver Death[f]	0.150
After Liver Transplant to Liver Death[f]	0.057
HCC First Year to Liver Death[c]	0.430
HCC Subsequent Year to Liver Death[c]	0.430
Viral Reinfection[e]	0.010

Sources: [a]Shepherd J, et al. *Health Technol Assess*. 2007;11:1-205; [b]Cardoso AC, et al. *J Hepatol*. 2010;52(5):652-7; [c]Hartwell D et al. *Health Technol Assess*. 2011;15(17):i-xii,1-210; Fattovich G, et al. *Gastroenterology*. 1997;112(2):463-472; [d]Hartwell D et al. *Health Technol Assess*. 2011;15(17):i-xii, 1-210; Grieve R, et al. *Gut*. 2006;55(9):1332-1338; Siebert U, et al. *Gut*. 2003;52(3):425-432; [e]Expert opinion; [f]Grieve R, et al. *Gut*. 2006;55(9):1332-1338; Bennett WG, et al. *Ann Intern Med*. 1997;127(10):855-865.

POPULATION CHARACTERISTICS

- Baseline characteristics of the target population were based on review of UK-based literature (**Table 2**)

Table 2. Baseline Patient Characteristics

Baseline Characteristics	Treatment-naïve GT1/GT4 Population
Mild (F0–1)	46%
Moderate (F2–3)	44%
CC (F4)	10%
Mean Age (in Years)	40
Male	70%

Source: Hartwell D et al. *Health Technol Assess.* 2011;15(17):i-xii, 1-210; Harris KA, et al. *J Med Virol*. 1999;58(2):127-131.

TREATMENT EFFICACY

- Efficacy rates were based on Phase 3 clinical trials with 3D ± RBV for treatment of GT1 treatment-naïve patients, and on the Phase 2 PEARL-I clinical trial with 2D ± RBV for treatment of GT4 treatment-naïve patients (**Table 3**)

Table 3. SVR Rates from AbbVie Clinical Trials

Baseline Characteristics	Mild (F0–1)	Moderate (F2–3)	CC (F4)
GT1	97.2%	97.2%	96.3%
GT4	100%	100%	97.9%

GT1 sources: SAPPHIRE I[12]; PEARL IV[13]; TURQUOISE II[14]; PEARL III[13].
GT4 source: PEARL I (CSR data).

OUTCOMES

- Health outcome measures included lifetime risks of DCC, HCC, LT, and LrD
- Other outcome measures included lifetime costs (i.e. drug and medical costs) and quality-adjusted life years (QALYs)
- Cost-effectiveness was quantified as incremental cost-effectiveness ratios (ICERs)
- Direct costs by health state were measured in UK pounds and based on a systematic literature review (**Table 4**)
- Costs and outcomes (e.g., QALYs) were discounted at 3.5%

Table 4. Direct Costs of HCV by Health State

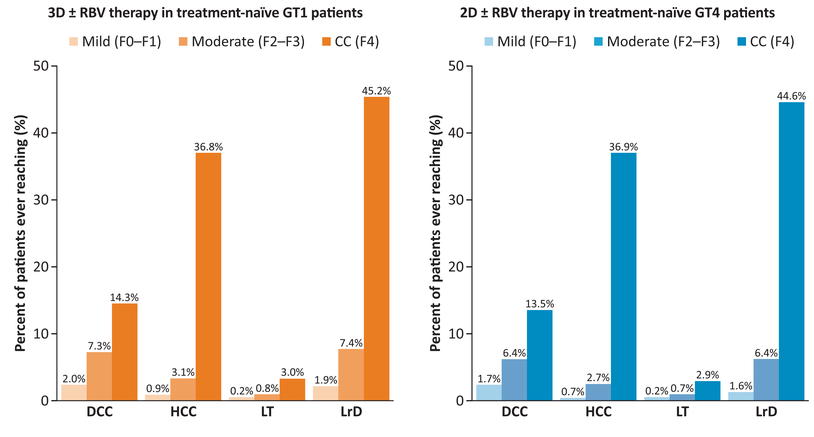
Variable	Annual Cost
Mild[a]	£160
Moderate[b]	£589
CC (Chronic HCV)[b]	£914
SVR, no HCV, history of mild fibrosis[b]	£58
SVR, no HCV, history of moderate fibrosis[b]	£58
SVR, no HCV, history of severe fibrosis (CC)[b]	£586
DCC[a]	£12,333
HCC (first year)[a]	£10,990
HCC (subsequent year)[a]	£10,990
Liver transplant (first year)[a]	£49,749
Liver transplant (subsequent years)[a]	£1,873

Sources: [a]Hartwell D et al. *Health Technol Assess*. 2011;15(17):i-xii, 1-210; [b]Backx M et al. *J Viral Hepat*. 2014;21(3):208-15.

RESULTS

- GT1- and GT4-HCV-infected patients who were treated with 3D ± RBV and 2D ± RBV, respectively, earlier in the disease have lower lifetime risk of DCC, HCC, LT, and LrD compared with patients treated at later fibrosis stages (**Figure 2**)

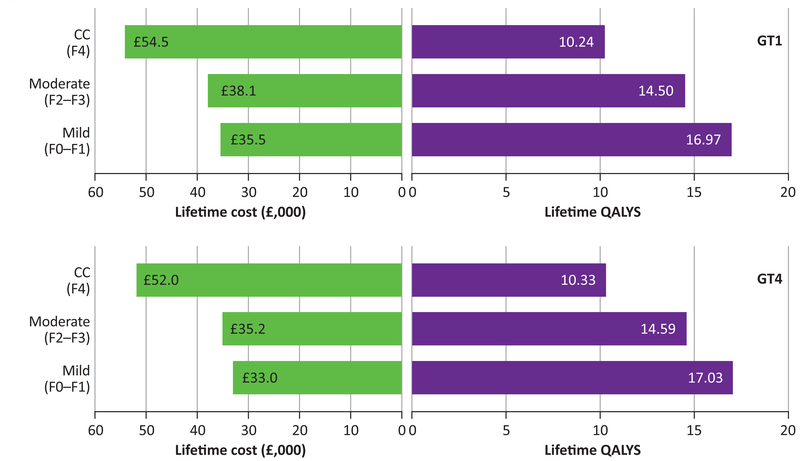
Figure 2. Lifetime Risk of DCC, HCC, LT, and LrD with HCV Treatment at Different Fibrosis stages



COST EFFECTIVENESS

- In both GT1 and GT4 treatment-naïve patients, initiation of treatment at more severe liver disease states resulted in greater lifetime costs and lower QALYs (**Figure 3**)

Figure 3. Lifetime Costs and QALYs with 3D ± RBV Treatment (GT1) / 2D ± RBV Treatment (GT4) at Different Fibrosis Stages



- Early treatment strategies were cost effective, and dominant (more QALYs gained at a lower cost) compared with treating at later fibrosis stages (**Table 5**)

Table 5. Cost-Effectiveness Analysis

		ICER vs CC	ICER vs Moderate	Dominant Treatment Strategy
GT1	Mild (F0–F1)	−£2,825	−£1,045	Mild dominant
	Moderate (F2–F3)	−£3,856		Moderate dominant
GT4	Mild (F0–F1)	−£2,829	−£905	Mild dominant
	Moderate (F2–F3)	−£3,929		Moderate dominant

Dominant = more QALYs at lower cost. ICER: Incremental cost-effectiveness ratio, £ per QALY.

DISCUSSION

- In the UK, the National Health Service (NHS) operates a fixed-budget, centrally-based, commissioning policy for HCV treatments which limits the number of eligible patients who can receive direct-acting antiviral therapy
- The eligible patient population has been previously restricted to include only patients with more severe liver disease (METAVIR F3 and F4)
- While access is now unrestricted in terms of fibrosis score (METAVIR F0–F4), the limiting step is the annual cap (run rate) in patients treated in order to keep within the budget threshold
- This analysis justifies a cost effectiveness argument for expanding eligibility criteria to include early stage treatment, but should be accompanied by increasing capacity (run rate) to treat patients regardless of fibrosis score

LIMITATIONS

- SVR inputs are obtained from AbbVie clinical trials and may differ from rates observed in a real-world setting
- Results for GT4 F4 patients are imputed from the PEARL-I clinical trial, as analysis was conducted prior to AGATE-I trial data availability. SVR rates were assumed equal to GT1b patients treated with 2D + RBV for 24 weeks as there is no data available for GT4 F4 patients
- 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
- While our findings are based on treatment-naïve patients, similar results were obtained for treatment-experienced patients
- Results may not be generalizable to specific real-world settings

CONCLUSIONS

- GT1- and GT4-HCV-infected patients who are treated with 3D ± RBV and 2D ± RBV earlier in the disease process have reduced risk of liver-related morbidity and mortality
- Treatment in early fibrosis stages is not only cost-effective, but also a dominant strategy as it provides greater QALY benefits at lower costs

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. Yuri Sanchez Gonzalez and Claire Lindsay are employees of AbbVie Inc. and may own stocks and/or options of the company. Andy Ingram is a contractor at Abbvie Inc. Suchin Virabhak is employed by Medicus Economics LLC, which received payment from AbbVie Inc. to undertake research. Hélène Parisé is a contractor to Medicus Economics LLC, which received payment from AbbVie Inc. to undertake research.

ACKNOWLEDGEMENT

Editorial support for poster development was provided by Tom Owen, PhD, of Fishawack Facilitate, and funded by AbbVie.

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Potential effect of hepatitis C treatment on renal, cardiovascular and metabolic extrahepatic manifestations: Results from clinical trials of ombitasvir/paritaprevir/ritonavir and dasabuvir ± ribavirin

THU-254

Tram T. Tran[1], Darshan Mehta[2,3], Andrea Goldstein[3], Eric Cohen[3], Yanjun Bao[3], Yuri Sanchez Gonzalez[3]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, United States; [2]Schaeffer Center for Health Policy and Economics, University of Southern California, CA, United States; [3]AbbVie Inc., North Chicago, IL, United States

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

- Hepatitis C virus (HCV) is both a hepato- and lymphotropic virus[1]
- Most HCV-infected patients are at risk of developing liver-related complications; however, HCV infection is also associated with the development of extrahepatic manifestations (EHMs)[2]
- Studies have shown that approximately two-thirds of HCV-infected patients experience EHMs[3]
- Benign mixed cryoglobulinaemia and B-cell lymphomas are the most frequently recognised EHMs, although other EHMs have been reported, including cardiovascular, metabolic, and renal diseases[4]
- The effects of the newer direct-acting antiviral (DAA) treatments on EHM-related outcomes are not well understood

OBJECTIVES

- To determine the impact of treatment with ombitasvir/paritaprevir (identified by AbbVie and Enanta)/ritonavir and dasabuvir ± ribavirin (3D±RBV) on cardiovascular, metabolic, and renal EHMs in HCV genotype 1-infected patients
- To investigate the differential effect of 3D±RBV treatment in clinically relevant subgroups based on EHM severity

METHODS

STUDY DESIGN

- We conducted a *post-hoc* analysis of clinical trial data from six Phase 3a trials investigating 3D±RBV[5–9]
- Data were pooled from all six trials

PATIENTS

- Study populations were defined as follows:
  - SP1: All HCV-infected patients treated with 3D±RBV regimen for 12 weeks in the placebo-controlled SAPPHIRE I and II trials[5,6]
  - SP2: All HCV-infected patients treated with placebo for 12 weeks, followed by 12 weeks of 3D±RBV regimen during the open-label period in the SAPPHIRE I and II trials[5,6]
  - SP3: All HCV-infected patients treated with 3D±RBV regimen for 12 or 24 weeks in the SAPPHIRE I and II, PEARL II, III, and IV, and TURQUOISE II trials[5–9]

EXTRAHEPATIC MANIFESTATIONS

- The following EHMs were studied: cardiovascular, metabolic, and renal diseases
- Each EHM was analysed collectively as a group using the following biomarkers, respectively: fasting triglyceride levels, fasting glucose levels, and estimated glomerular filtration rates (eGFR)

STATISTICAL ANALYSIS

- Treatment effects were measured using longitudinal mixed model (MM) regression analyses, which were performed for each EHM with the respective biomarker values at each time point as the main dependent variable
  - The main explanatory variable was whether patients were in the treatment (SP1) or placebo group (SP2)
  - Patient biomarker measurements at baseline, demographics, and clinical characteristics were included as fixed effect covariates
  - Study enrolment was treated as a random effect
- The SP3 population was used to study the differential effect of HCV treatment with 3D±RBV by clinically relevant subgroups using MM analyses for each EHM
  - The subgroups for each EHM were defined by baseline biomarker levels (**Table 1**)
- The change from baseline at subsequent time points was estimated and plotted based on the regression predictions (ie, fitted values) from the MM analysis

Table 1. Clinically Relevant Subgroups for Each EHM

EHM Subgroup	Subgroup Definition[a]	Sample Size, n (%)
Cardiovascular		
Normal triglyceride levels	Fasting triglycerides levels <150 mg/dL	1499 (86.4)
Elevated triglyceride levels	Fasting triglyceride levels ≥150 mg/dL	236 (13.6)
Metabolic		
Normal glucose levels	Fasting glucose levels <100 mg/dL	1192 (68.7)
Pre-diabetes	Fasting glucose levels 100–126 mg/dL	440 (25.4)
Diabetes	Fasting glucose levels >126 mg/dL	103 (5.9)
Renal		
CKD stage 1	eGFR >90 mL/min/1.73 m^2	820 (41.9)
CKD stage 2	eGFR 60–89 mL/min/1.73 m^2	1091 (55.8)
CKD stage 3 and higher[b]	eGFR ≤59 mL/min/1.73 m^2	44 (2.2)

[a]Biomarker values measured at baseline. [b]Of 44 patients: 38 patients were CKD stage 3a, 4 patients were CKD stage 3b, and 1 patient was CKD stage 4. CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; EHM=extrahepatic manifestation.

Table 2. Patient Demographics and Clinical Characteristics at Baseline

	Cardiovascular and Metabolic EHMs[a]			Renal EHMs[b]		
EHM Subgroup	**SP1**	**SP2**	**SP3**	**SP1**	**SP2**	**SP3**
n	630	199	1735	776	255	2015
Age, years, mean (SD)	50.1 (10.8)	52.1 (10.2)	51.5 (10.9)	50.3 (10.8)	52.6 (9.7)	51.6 (10.8)
Sex, %						
Male	56.0	52.3	58.2	57.2	52.2	57.8
Race, %						
White	90.6	90.5	90.8	90.7	90.6	93.9
Black	6.3	6.5	6.5	6.4	7.1	6.2
Asian	2.4	1.5	1.7	2.2	1.2	1.7
Others	0.6	1.5	1.0	0.6	1.2	0.8
Region/Countries, %						
North America	47.0	38.7	45.7	47.6	42.0	46.6
Europe	48.1	55.3	52.5	46.8	51.4	51.3
Australia/New Zealand/ Other	4.9	6.0	1.8	5.7	6.7	2.1
Fibrosis, %						
F0–F1	74.9	72.9	57.9	73.1	71.0	57.7
F2	15.7	16.1	14.3	16.1	17.3	14.4
F3	9.4	11.1	9.3	10.8	11.8	9.9
F4	0.0	0.0	18.5	0.0	0.0	18.0
HCV subgenotype,[c] %						
1A	63.2	59.3	49.2	64.4	63.5	50.8
HCV viral load, %						
≥800,000 IU/mL[d]	80.8	84.4	81.7	81.2	85.5	81.7
BMI,[e] %						
<30 kg/m^2	83.8	82.9	80.9	83.1	80.4	80.8
Prior diabetes history,[f] %						
Yes	4.4	4.5	7.3	4.4	3.5	7.0
HOMA-IR,[g] %						
≥3	18.1	17.6	26.6	14.8	13.7	22.1
Missing	7.8	9.0	6.7	24.4	28.6	21.2
HCV history, %						
Treatment naïve	61.0	61.8	65.6	61.6	62.0	66.1
P/R experienced	39.0	38.2	34.4	38.4	38.0	33.9
SVR12,[h] %	96.8	94.5	96.5	95.6	93.3	98.4

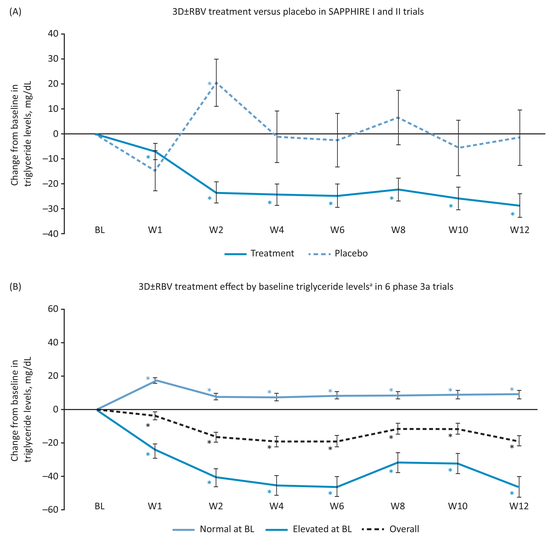
[a]In the cardiovascular and metabolic EHM group, n represents the total number of patients with evaluable fasting triglycerides and glucose values at baseline (both biomarkers were measured at baseline in the same patient population). Patients with non-fasting values at baseline were excluded from the analysis. [b]In the renal EHM group, n represents the total number of patients with evaluable eGFR values at baseline. [c]For subgenotype, the remaining percentage represents HCV 1B. [d]Remaining percentage of patients had a baseline viral load <800,000 IU/mL. [e]For BMI, the remaining percentage represents ≥30 kg/m^2. [f]For prior diabetes history, the remaining percentage represents no diabetes. [g]For HOMA-IR, the remaining percentage represents <3. [h]For SVR12, the remaining percentage represents no attainment of SVR12. BMI=body mass index; EHM=extrahepatic manifestation; HCV=hepatitis C virus; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; P/R=peginterferon/ribavirin; SVR12=sustained virological response at 12 weeks. SP1: All HCV-infected patients treated with 3D±RBV regimen for 12 weeks in the placebo-controlled SAPPHIRE I and II trials; SP2: All HCV-infected patients treated with placebo for 12 weeks, followed by 12 weeks of 3D±RBV regimen during the open-label period in the SAPPHIRE I and II trials; SP3: All HCV-infected patients treated with 3D±RBV regimen for 12 or 24 weeks in the SAPPHIRE I and II, PEARL II, III, and IV, and TURQUOISE II trials.

RESULTS

CARDIOVASCULAR MANIFESTATIONS

- Adjusted mean triglyceride levels at week 12 were significantly (p=.024) lower in patients treated with 3D±RBV than placebo (**Figure 1A**)
  - Patients treated with 3D±RBV (SP1) had statistically significant decreases in triglyceride levels compared with baseline at each time point. In contrast, at nearly all time points, triglyceride levels did not change significantly from baseline in patients treated with placebo (SP2)
- Among the overall treated sample from six Phase 3a trials (SP3), treatment with 3D±RBV resulted in statistically significant decreases in triglyceride levels compared with baseline at all time points (–20 mg/dL by week 12; p<.0001) (**Figure 1B**)
  - Subgroup analysis by EHM severity showed that patients with elevated triglyceride levels at baseline had large and significant decreases from baseline in triglyceride levels (–48.3 mg/dL by week 12; p<.0001)
  - Patients with normal triglyceride levels showed modest but significant increases in triglyceride levels (7.18 mg/dL by week 12; p=.001)

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

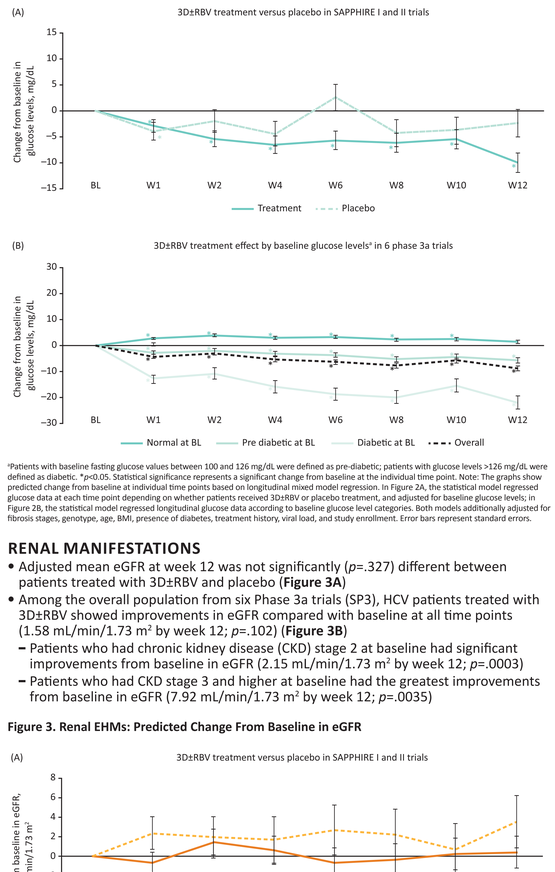


[a]Fasting baseline triglyceride levels ≥150 mg/dL were defined as elevated. *p<0.05. Statistical significance represents a significant change from baseline at the individual time point. Note: The graphs show predicted change from baseline at individual time points based on longitudinal mixed model regression. In Figure 1A, the statistical model regressed triglyceride data at each time point depending on whether patients received 3D±RBV or placebo treatment, and adjusted for baseline triglyceride levels; in Figure 1B, the statistical model regressed longitudinal triglyceride data according to baseline triglyceride level categories. Both models additionally adjusted for fibrosis stages, genotype, age, BMI, presence of diabetes, treatment history, viral load, and study enrollment. Error bars represent standard errors.

METABOLIC MANIFESTATIONS

- Adjusted mean glucose levels at week 12 were significantly (p=.021) lower in HCV patients treated with 3D±RBV than placebo (**Figure 2A**)
  - Patients treated with 3D±RBV (SP1) had statistically significant decreases in glucose levels compared with baseline at each time point. In contrast, glucose levels did not change significantly from baseline post week 1 in patients treated with placebo (SP2)
- Among the overall treated sample from six Phase 3a trials (SP3), treatment with 3D±RBV resulted in statistically significant decreases in glucose levels compared with baseline at all time points (–8.87 mg/dL by week 12; p<.0001) (**Figure 2B**)
  - Patients who had pre-diabetes at baseline had significant decreases from baseline in glucose levels (–5.78 mg/dL by week 12; p<.0001)
  - Patients who had diabetes at baseline had the greatest decreases from baseline in glucose levels (–22.1 mg/dL by week 12; p<.0001)
  - Patients with normal glucose levels demonstrated small but non-significant increases in glucose levels (1.34 mg/dL by week 12; p=.057)

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

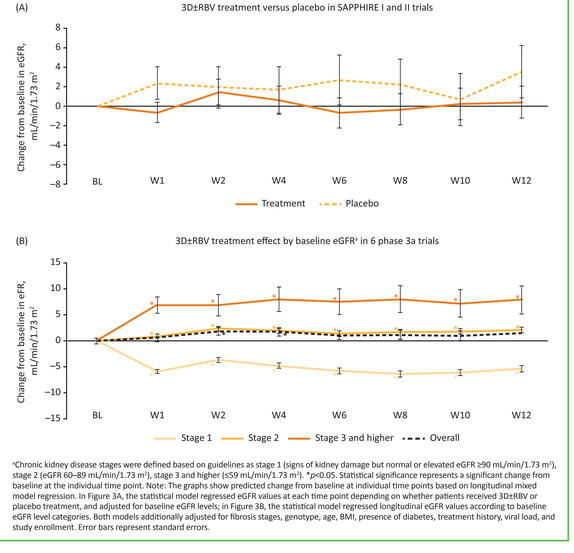


[a]Patients with baseline fasting glucose values between 100 and 126 mg/dL were defined as pre-diabetic; patients with glucose levels >126 mg/dL were defined as diabetic. *p<0.05. Statistical significance represents a significant change from baseline at the individual time point. Note: The graphs show predicted change from baseline at individual time points based on longitudinal mixed model regression. In Figure 2A, the statistical model regressed glucose data at each time point depending on whether patients received 3D±RBV or placebo treatment, and adjusted for baseline glucose levels; in Figure 2B, the statistical model regressed longitudinal glucose data according to baseline glucose level categories. Both models additionally adjusted for fibrosis stages, genotype, age, BMI, presence of diabetes, treatment history, viral load, and study enrollment. Error bars represent standard errors.

RENAL MANIFESTATIONS

- Adjusted mean eGFR at week 12 was not significantly (p=.327) different between patients treated with 3D±RBV and placebo (**Figure 3A**)
- Among the overall population from six Phase 3a trials (SP3), HCV patients treated with 3D±RBV showed improvements in eGFR compared with baseline at all time points (1.58 mL/min/1.73 m^2 by week 12; p=.102) (**Figure 3B**)
  - Patients who had chronic kidney disease (CKD) stage 2 at baseline had significant improvements from baseline in eGFR (2.15 mL/min/1.73 m^2 by week 12; p=.0003)
  - Patients who had CKD stage 3 and higher at baseline had the greatest improvements from baseline in eGFR (7.92 mL/min/1.73 m^2 by week 12; p=.0035)

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



[a]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). *p<0.05. Statistical significance represents a significant change from baseline at the individual time point. Note: The graphs show predicted change from baseline at individual time points based on longitudinal mixed model regression. In Figure 3A, the statistical model regressed eGFR values at each time point depending on whether patients received 3D±RBV or placebo treatment, and adjusted for baseline eGFR levels; in Figure 3B, the statistical model regressed longitudinal eGFR values according to baseline eGFR level categories. Both models additionally adjusted for fibrosis stages, genotype, age, BMI, presence of diabetes, treatment history, viral load, and study enrollment. Error bars represent standard errors.

DISCUSSION

- The biomarker levels used in the current study to evaluate EHMs have been associated with varying risks of clinical outcomes
  - Elevated triglyceride levels have been associated with increased risk of coronary heart disease and all-cause mortality[10,11]
  - Elevated glucose levels have been associated with higher rates of cardiovascular events[12,13]
  - Decreases in eGFR have been associated with increased risk for end-stage renal disease (ESRD) and absolute all-cause mortality[14]
- The overall improvements in biomarker levels observed in the current study for all HCV patients treated with the 3D±RBV regimen, especially in patients with advanced EHM severity at baseline, may indicate long-term clinical benefits including:
  - Lowered risk of coronary heart disease and all-cause mortality in cardiovascular manifestations
  - Delayed development of metabolic syndrome and associated cardiovascular events in metabolic manifestations
  - Reduced risk for ESRD and all-cause mortality in renal manifestations
- These results are in line with previously published literature where HCV viral eradication with interferon/RBV based regimen has been associated with a lower risk of cardiovascular complications,[15] prevention or delay of the onset of metabolic syndrome,[16] and lowered risk of ESRD development[15]

LIMITATIONS

- This analysis used data from patients enrolled in clinical trials and therefore may have limited generalizability to the overall HCV-infected population
- Unobserved confounding variables not included in regression analyses can potentially bias the study results. However, to study the effect of HCV treatment on EHM outcomes, we utilised data from patients randomly assigned to HCV treatment and placebo, which may help mitigate this concern to a large extent
- The relationship between the biomarkers used in the analysis and clinical EHM outcomes was extrapolated based on prior published literature and further analyses (e.g. long-term real world data with confirmed diagnoses or outcomes) are warranted to confirm these findings
- The current study followed patients during the treatment period only. Therefore, the persistency of EHM outcomes was not established post treatment

CONCLUSIONS

- Treatment with 3D±RBV demonstrates an association with EHM improvements in HCV-infected patients. These results are in line with the beneficial effects observed in patients treated with interferon/RBV regimens
- Unlike other DAA regimens,[17,18] the results from this study showed no negative effect of 3D±RBV treatment on renal function
- HCV-infected patients with advanced EHMs may benefit most from DAA therapy

DISCLOSURES

Design and study conduct for the study were 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 publication and maintained control over the final content. **Conflicts of Interest: Tram Tran** received consulting, advisor/speaker fees, and research grants from Gilead Sciences, Bristol-Myers Squibb, and AbbVie. **Darshan Mehta** was financially supported for graduate research work by AbbVie Inc. as part of a fellowship agreement between AbbVie and the University of Southern California. **Andrea Goldstein**, **Eric Cohen**, **Yanjun Bao**, and **Yuri Sanchez Gonzalez** are employees of AbbVie Inc. and may own stocks and/or options of the company.

ACKNOWLEDGEMENT

Editorial support for poster development was provided by Paul MacCallum, PhD of Fishawack Facilitate and funded by AbbVie Inc.

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Extra-hepatic manifestations from hepatitis C virus infection related to female infertility and adverse pregnancy outcomes: A real-world observation

SAT-295

Erica Villa[1], Xue Han[2], Andrea S. Goldstein[3], Shivaji Manthena[3], Yanjun Bao[3], Yuri Sanchez Gonzalez[3]

[1]Division of Gastroenterology, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy; [2]Leonard D. Schaeffer Center, University of Southern California (USC), Los Angeles, CA, USA; [3]AbbVie Inc., North Chicago, IL, USA

Presented at the European Association for the Study of the Liver (EASL), April 19 – 23, 2017, Amsterdam, Netherlands

BACKGROUND

- The majority of new hepatitis C virus (HCV) infections is among injecting drug users, some of whom are young women in their childbearing years[1,2]
- HCV infection may have an effect on ovarian senescence in women of reproductive age[3]
- Although there is a growing body of evidence on the extra-hepatic manifestations (EHMs) that are secondary to HCV-related inflammatory responses and/or autoimmune reactions,[4–9] further evidence is needed on the potential link HCV infection may have with female infertility and pregnancy outcomes

OBJECTIVES

- To assess the relationship between HCV infection and female infertility and pregnancy outcomes in a large real-world population in the United States (US)

METHODS

DATA SOURCE: US CLAIMS DATABASE

- Large de-identified US insurance claims database containing patient-level medical, prescription, and laboratory data from 2000 to 2015
- Patient enrolment information was used to identify periods of continuous eligibility for each patient
- Patient demographic information included year of birth, sex, and geographic regions
- All patient-level data met the Health Insurance and Portability and Accountability Act (HIPAA) requirements for fully de-identified datasets

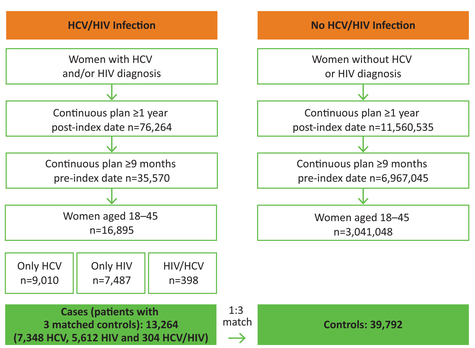
OUTCOMES

- Rates of female infertility associated with HCV mono-infection, HIV mono-infection, and HCV/HIV co-infection compared with non-HCV- or HIV-infected controls
- Rates of premature birth, live birth, stillbirth, gestational diabetes, pre-eclampsia, and miscarriage associated with HCV infection in pregnant women compared with non-HCV-infected controls

STUDY DESIGN: INFERTILITY ANALYSIS (FIGURE 1)

- Inclusion criteria
  - Women 18–45 years of age
  - No pregnancy
  - HCV mono-infection, HIV mono-infection, and HCV/HIV co-infection diagnosis based on International Classification of Diseases, 9th Revision (ICD-9) codes for HCV and HIV

Figure 1. Sample Selection: Infertility Analysis

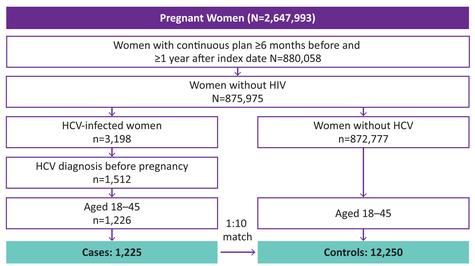


- ICD-9 codes: HCV (070.41, 070.44; 070.51, 070.54, 070.70, 070.71, V02.62); HIV (042, 043, 044, 079.53, 795.71, V08)
- Index date
  - HCV mono-infection: date of first HCV diagnosis
  - HIV mono-infection: date of first HIV diagnosis
  - HIV/HCV co-infection: date of first HCV or HIV diagnosis
  - Control group: random date
- ≥9 months continuous enrolment before and ≥1 year after index date
- Case-control matching
  - Cases: HCV mono-infection, HIV mono-infection, and HCV/HIV co-infection
  - Controls: No HCV or HIV infection
  - Cases matched to controls in a 1:3 ratio based on age, region, year of index date, and enrolment period
- Infertility was identified using ICD-9 codes (628.0–628.4, 628.8, 628.9, V26.21, V26.29, V26.81, V26.82, V59.70–V59.74)

STUDY DESIGN: PREGNANCY OUTCOMES ANALYSIS (FIGURE 2)

- Inclusion criteria
  - Pregnant women 18–45 years of age
  - At least 1 pregnancy diagnosis based on ICD-9 code (V22.0–V24.2, V72.42)
  - ≥6 months continuous enrolment before and ≥1 year after index date
  - HCV diagnosis based on ICD-9 codes
- Index date: date of pregnancy diagnosis
- Case-control matching
  - Cases: HCV mono-infection
  - Controls: No HCV or HIV infection
  - Cases matched to controls in a 1:10 ratio based on age, region, year of index date, and enrolment period
- Pregnancy outcomes were identified using the following ICD-9 codes:
  - Premature birth (644.0, 644.03, 644.20, 644.21), live birth without complications (V27.0, V27.2, V27.5, V30.0, V31.0, V34.0, V39.0), stillbirth (V27.3, V27.6, V32.0, V35.0, V36.0), gestational diabetes (648.83), pre-eclampsia (642.4x, 642.5x, 642.6x, 642.7x), and miscarriage (634.xx)

Figure 2. Sample Selection: Pregnancy Outcomes Analysis



DATA ANALYSES

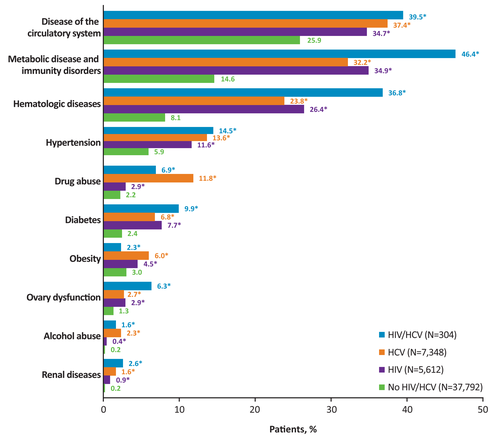
- Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regressions to examine the association between:
  - HCV mono-infection, HIV mono-infection, or HCV/HIV co-infection and risk of infertility (vs no HCV/HIV infection)
  - HCV mono-infection and risk of premature birth, live birth, stillbirth, gestational diabetes, pre-eclampsia, and miscarriage (vs no HCV infection)
- Covariates included age, geographic region, year of index date, type of health plan, and comorbidities (identified per ICD-9 codes)

RESULTS

COMORBIDITIES IN INFERTILITY ANALYSIS POPULATION

- A greater proportion of HCV- and/or HIV-infected women had comorbidities compared with women who were not infected with HCV or HIV (**Figure 3**)
- Consistent with previous literature,[4–9] some of these comorbidities include EHMs, such as renal, circulatory system, metabolic and hematologic diseases, immunity disorders, hypertension, diabetes, and ovarian dysfunction

Figure 3. Comorbidities in Infertility Analysis



*p<0.01, joint significance test for group differences.

INFERTILITY RATES (TABLE 1)

- HIV mono-infection, HCV mono-infection, and HIV/HCV co-infection were associated with greater rates of infertility vs no HCV or HIV infection

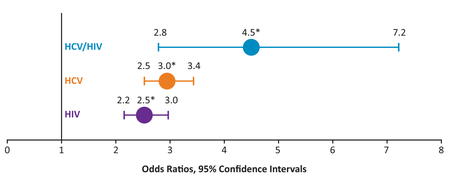
Table 1. Rates of Infertility

Outcome, n (%)	No HIV/HCV Cohort (N=39,792)	HIV Cohort (N=5,612)	HCV Cohort (N=7,348)	HIV/HCV Cohort (N=304)
Infertility	660 (1.7)	265 (4.7)	307 (4.2)	26 (8.6)

ODDS OF INFERTILITY (FIGURE 4)

- While HCV mono-infection (OR=3.0; 95% CI: 2.5, 3.4) and HIV mono-infection (OR=2.5; 95% CI: 2.2, 3.0) are associated with significantly greater odds of infertility compared with no HCV or HIV infection, HIV and HCV co-infection further significantly increased the odds of infertility (OR=4.5; 95% CI: 2.8, 7.2)

Figure 4. Adjusted Odds of Infertility With HCV/HIV Co-infection, HCV Mono-infection, or HIV Mono-infection Versus No HCV or HIV Infection

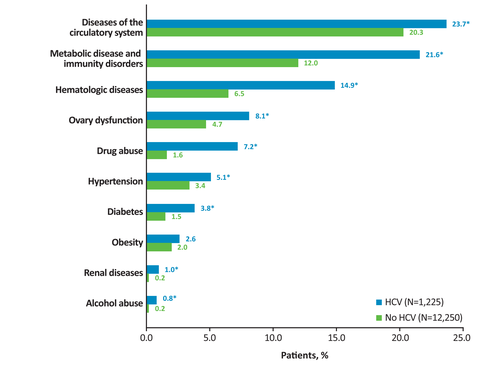


HCV/HIV: N=308; HCV: N=7,348; HIV: N=5,612; No HIV/HCV: N=39,792
*p<0.0001 based on multivariate regression analysis; covariates included age, geographic region, year of index date, type of health plan, and comorbidities; reference group: no HCV/HIV.

COMORBIDITIES IN PREGNANCY OUTCOMES ANALYSIS POPULATION

- A greater percentage of pregnant women infected with HCV had EHMs and other comorbidities compared with pregnant women who were not infected with HCV (**Figure 5**)

Figure 5. Comorbidities in Pregnancy Outcomes Analysis



*p<0.01; reference group: no HCV.

ADVERSE PREGNANCY OUTCOME RATES (TABLE 2)

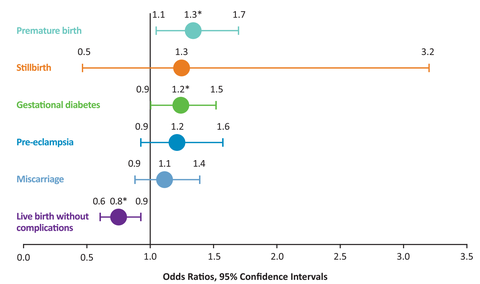
Table 2. Rates of Adverse Pregnancy Outcomes

Outcome, n (%)	Pregnant HCV Cohort (N=1,225)	Pregnant No HCV Cohort (N=12,250)
Premature birth	91 (7.4)	696 (5.7)
Live birth without complications	537 (43.8)	6,732 (55.0)
Stillbirth	5 (0.4)	47 (0.4)
Gestational diabetes	131 (10.7)	1,102 (9.0)
Pre-eclampsia	74 (6.0)	640 (5.2)
Miscarriage	106 (8.7)	1,096 (9.0)

ODDS OF ADVERSE PREGNANCY OUTCOMES (FIGURE 6)

- Among the 13,475 pregnant women included in the analysis of pregnancy outcomes, HCV-infected women were significantly more likely to have premature birth (OR=1.3; 95% CI: 1.1, 1.7) and gestational diabetes (OR=1.2; 95% CI: 1.0, 1.5), and significantly less likely to have a live birth without complications (OR=0.8; 95% CI 0.6, 0.9) than women who were not infected with HCV
- Odds of stillbirth (OR=1.3; 95% CI: 0.5, 3.2), pre-eclampsia (OR=1.2; 95% CI: 0.9, 1.6), and miscarriage (OR=1.1; 95% CI: 0.9, 1.4) were not statistically different than 1

Figure 6. Adjusted Odds of Adverse Pregnancy Outcomes in HCV-infected Women Versus No HCV Infection



HCV: N=1,225; No HCV: N=12,250
*p<0.05 based on multivariate regression analysis; covariates included age, geographic region, year of index date, type of health plan, and comorbidities; reference group: no HCV.

DISCUSSION

- Risks of infertility and adverse pregnancy outcomes were significantly increased in women infected with HCV
- ORs for some pregnancy outcomes were not statistically significant owing to a small sample size
- It is unclear to what extent viral suppression with therapy could mitigate these risks

LIMITATIONS

- Women filling HCV prescriptions outside the available pharmacy coverage plan are included in the no-HCV treatment group, which may confound and underestimate the actual effect of HCV infection
- The rate of live births without complications in this study is less than the national live birth rate (55% vs 65%),[10] plausibly due to missing pregnancy data associated with the use of claims data
- Results may further be confounded due to factors not included in the matching approach or as covariates
- Given the natural limitations of claims data, results may not be generalizable to patient populations beyond the study sample

CONCLUSIONS

- In a real-world analysis, HCV is associated with increased burden for women of childbearing age in terms of infertility and adverse pregnancy outcomes, including stillbirths and gestational diabetes and fewer live births without complications
- Given these risks, early treatment of HCV-infected women of childbearing age should be considered

DISCLOSURES

Erica Villa is an employee of the Azienda Ospedaliero-Universitaria Policlinico di Modena and a consultant for AbbVie Inc. She is also a consultant for GSK, Novartis, MSD, and BMS, and her institution has received research support from AbbVie Inc. and Roche. Xue Han is a doctoral student at the University of Southern California and served as an AbbVie Inc. intern during the time when the study was conducted.

Andrea S. Goldstein, Yanjun Bao, Shivaji Manthena, and Yuri Sanchez Gonzalez are employees of AbbVie Inc. and may own stocks and/or options of the company.

ACKNOWLEDGEMENT

Design, study conduct, and financial support for the study were provided by AbbVie Inc. AbbVie Inc. participated in the interpretation of data, review, and approval of the poster; all authors contributed to the development of the publication and maintained control over the final content. Medical writing support was provided by Joann Hettasch, PhD, Fishawack Group of Companies, Conshohocken, PA; this support was funded by AbbVie Inc.

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