Healthcare resource use (HCRU) and cost impact of potential drug-drug interactions (DDIs) among HCV patients receiving direct-acting antivirals (DAAs) concomitantly with antipsychotic drugs in the US

WED-031

Dilip Makhija,[1] Thomas Debray,[2] Candido Hernández[3]

[1]Gilead Sciences, Parsippany, United States of America, [2]Smart Data Analysis and Statistics, Utrecht, Netherlands, [3]Gilead Sciences, S.L.U, Madrid, Spain

Conclusions

- Despite HCV treatment guidelines from EASL and AASLD recommending the use of the Liverpool DDI tracker before initiating DAA therapy, PI-based DAAs (such as GLE/PIB), which show an increased risk of DDIs, are commonly used for HCV patients receiving concomitant antipsychotics in the US, as compared to a PI-free regimen such as SOF/VEL
- This analysis demonstrates the importance of safety monitoring for patients and the need for individualized medicine to ensure an appropriate DAA is used, to minimize HCRU and cost implications for patients with polypharmacy
- Specifically, the results highlight that mean all-cause and HCV-related healthcare costs PPPM were numerically lower for SOF/VEL patients versus GLE/PIB, and all-cause outpatient costs PPPM were statistically lower for SOF/VEL
- Additional research into the HCRU and cost implications in those with HCV at risk of DDIs is needed to further investigate this relationship

Introduction and Objectives

- Psychiatric illnesses occur frequently in patients with chronic hepatitis C virus (HCV) infection; consequently, concomitant use of antipsychotic medications with DAAs may be necessary[1]
- The importance of evaluating this co-use lies in the risk of DDIs, the associated impact on patient safety, and the potential for an increase in HCRU[2,3]
- The European Association for the Study of the Liver (EASL) recommends assessing potential DDIs with concomitant medications before initiating DAA therapy, using resources like the University of Liverpool DDI tracker.[4,5] Similarly, the American Association for the Study of Liver Diseases (AASLD) endorses this tool in their Hepatitis C Point of Care Test and Treat Algorithm for medication reconciliation prior to treatment initiation[6]
- Data on the use of HCV therapy with DAAs concomitantly with antipsychotic medications has been described across Europe and Asia; however, limited information on this co-use and the impact of DDIs exists in the United States (US)
- The objective of this study was to use a US claims database to explore concomitant use of antipsychotic medications (N05A as per Anatomical Therapeutic Chemical [ATC] classification) alongside two pangenotypic DAAs, sofosbuvir/velpatasvir (SOF/VEL) and glecaprevir/pibrentasvir (GLE/PIB), ultimately evaluating the risk of DDIs, quality of prescriptions, HCRU, and costs associated with this polypharmacy[7]

Methods

- This retrospective cohort study identified patients treated for chronic HCV in the US using data from 01 July 2015 to 30 June 2023 in the IQVIA PharMetrics Plus and IQVIA Ambulatory Electronic Medical Record databases
- Patients were included if they had a claim for SOF/VEL or GLE/PIB at the same time as a DDI-related medication (DDIRM). DDIRMs with fill length overlapping with SOF/VEL or GLE/PIB treatment were considered DDI-related comedications (DDIRCs)
- The analysis period for each patient was from the index date (start of HCV treatment) until 6 months (180 days)
- Potential DDIs were evaluated using the University of Liverpool Hepatitis Interactions database in May 2024, with the potential DDI risk classified according to:[5]

Strength of Interaction	DDI Risk
Do not coadminister (red)	Contraindicated
Potential clinically significant interaction (amber)	Clinically significant DDI
Potential weak interaction (yellow)	Weak DDI
No interaction (green)	No DDI risk

- Quality of prescriptions was assessed by calculating the proportion of patients without elevated DDI risk (i.e., patients who did not receive inappropriate prescriptions due to potential DDI concerns)
- Matched cohorts were created using 1:1 propensity score (PS) matching without replacement to compare HCRU and costs between SOF/VEL and GLE/PIB patients
  - PS matching accounted for age, sex, insurance status, HCV index year, weighted Charlson Comorbidity Index (CCI), and specific comorbidities (i.e., gastroesophageal reflux disease, epilepsy, and hyperlipidemia) as covariates
- HCRU (healthcare visits) and costs (mean and median per patient per month [PPPM]) were assessed during the study period for both all-cause and HCV-related outcomes
  - Mean HCRU and costs were analyzed using Poisson and Gamma generalized regression analyses, respectively

Results

DDI Risk (Total Cohort)

- A total of 11,324 patients were included; 6,784 (59.9%) treated with SOF/VEL and 4,540 (40.1%) with GLE/PIB. Of the total cohort, 3.7% (420/11,324) were receiving concomitant antipsychotics; 3.9% (267/6,784) of patients receiving SOF/VEL and 3.4% (153/4,540) receiving GLE/PIB
- Patients in the SOF/VEL total cohort had a higher mean age and weighted CCI score than the GLE/PIB cohort (**Table 1**)
- Among the 267 patients on SOF/VEL, weak or clinically significant DDI risk was present in 14.6% (39/267) of patients (13.1% [35/267] weak and 1.5% [4/267] clinically significant). For the 153 GLE/PIB treated patients, 100% had weak or clinically significant DDI risk (19.0% [29/153] weak and 83.7% [128/153] clinically significant)
- The quality of prescriptions was 98.5% (263/267) for SOF/VEL and 16.3% (25/153) for GLE/PIB (**Figure 1**)
- Most patients (94.5% [397/420]) received only one antipsychotic concomitantly while 5.5% (23/420) received >1 (5.2% [14/267] in SOF/VEL and 5.9% [9/153] in GLE/PIB), indicative of polypharmacy and potential multi-DDI risk
  - Regarding multi-DDI risk in those receiving >1 concomitant medication, no SOF/VEL treated patients received concomitantly two antipsychotics both showing DDI risk. The 9 GLE/PIB patients all received two antipsychotics showing DDI risk; in 5 patients both antipsychotics showed clinically significant DDI risk

HCRU and Costs (Propensity-Matched Cohort)

- The matched SOF/VEL and GLE/PIB cohorts each comprised 142 patients concomitantly receiving antipsychotics. All patient characteristics were similar between the SOF/VEL and GLE/PIB cohorts after PS matching (**Table 1**)
- The mean number of all-cause and HCV-related visits within 6 months after the initiation of DAA treatment was similar between SOF/VEL and GLE/PIB patients
- All patients incurred all-cause and HCV-related HCRU, with the majority of HCRU attributed to pharmacy visits (100% of SOF/VEL [142/142] and GLE/PIB [142/142]) patients had ≥1 all-cause pharmacy visit) and outpatient visits (15.5% [22/142] of SOF/VEL and 18.3% [26/142] of GLE/PIB patients had ≥1 all-cause outpatient visit)
  - The regression analysis showed that the odds of having all-cause or HCV-related visits were similar between SOF/VEL and GLE/PIB patients
- Mean (standard deviation [SD]) all-cause healthcare costs PPPM were numerically lower for SOF/VEL patients ($39 [71]) compared with GLE/PIB patients ($69 [210]); however, the difference was not statistically significant (p=0.07). In contrast, when examining specific components of healthcare costs, patients prescribed SOF/VEL had significantly lower (p=0.037) mean (SD) all-cause outpatient costs PPPM ($7 [21]) compared with GLE/PIB ($29 [151]). For the remaining outcomes (inpatient, emergency room, telehealth, pharmacy, and other visits), no significant differences were observed (**Figure 2**)
- Mean (SD) HCV-related healthcare costs PPPM were numerically lower for SOF/VEL patients ($33 [66]) compared with GLE/PIB patients ($41 [106]); however, the difference was not statistically significant (p=0.427; **Figure 2**)
- Median (interquartile range [IQR]) total all-cause and HCV-related PPPM costs were similar between SOF/VEL (all-cause: $13 [2; 36]; HCV-related: $12 [0; 28]) and GLE/PIB (all-cause: $15 [0; 49]; HCV-related: $10 [0; 32]) treated patients (**Figure 3**)
  - All-cause and HCV-related inpatient, emergency, outpatient, telehealth, and other visits had a median (IQR) cost of $0 (0; 0) for both cohorts

Table 1. Patient Characteristics

Characteristic		Total cohort			Propensity-matched cohort		
		SOF/VEL	GLE/PIB	p-value	SOF/VEL	GLE/PIB	p-value
n		267	153		142	142	
Age at index, mean (SD)		46.19 (13.54)	42.32 (13.15)	0.005	42.92 (13.10)	42.70 (13.38)	0.890
Gender, n (%)	Male	131 (49.1)	72 (47.1)	0.769	72 (50.7)	67 (47.2)	0.635
	Female	136 (50.9)	81 (52.9)		70 (49.3)	75 (52.8)	
Insurance, n (%)	Commercial	154 (57.7)	98 (64.1)	0.003	100 (70.4)	97 (68.3)	0.985
	Medicare	62 (23.2)	14 (9.2)		13 (9.2)	14 (9.9)	
	Medicaid	11 (4.1)	11 (7.2)		1 (0.7)	1 (0.7)	
	Self-Insured	40 (15.0)	30 (19.6)		28 (19.7)	30 (21.1)	
HCV index year, n (%)	2016	14 (5.2)	0 (0.0)	<0.001			
	2017	45 (16.9)	5 (3.3)		5 (3.5)	5 (3.5)	0.941
	2018	37 (13.9)	45 (29.4)		31 (21.8)	35 (24.6)	
	2019	37 (13.9)	30 (19.6)		28 (19.7)	29 (20.4)	
	2020	52 (19.5)	36 (23.5)		44 (31.0)	36 (25.4)	
	2021	65 (24.3)	27 (17.6)		24 (16.9)	27 (19.0)	
	2022	17 (6.4)	10 (6.5)		10 (7.0)	10 (7.0)	
CCI, weighted, mean (SD)		2.25 (1.78)	1.79 (1.36)	0.006	1.83 (1.48)	1.80 (1.36)	0.868
Gastroesophageal reflux disease, n (%)	No	189 (70.8)	111 (72.5)	0.785	107 (75.4)	102 (71.8)	0.590
	Yes	78 (29.2)	42 (27.5)		35 (24.6)	40 (28.2)	
Epilepsy, n (%)	No	256 (95.9)	143 (93.5)	0.389	137 (96.5)	135 (95.1)	0.768
	Yes	11 (4.1)	10 (6.5)		5 (3.5)	7 (4.9)	
Hyperlipidemia, n (%)	No	214 (80.1)	132 (86.3)	0.146	123 (86.6)	122 (85.9)	1.000
	Yes	53 (19.9)	21 (13.7)		19 (13.4)	20 (14.1)	

Figure 1. Patients in the Total Cohort with ≥1 Claim with DDI Risk by Cohort and Rating Level

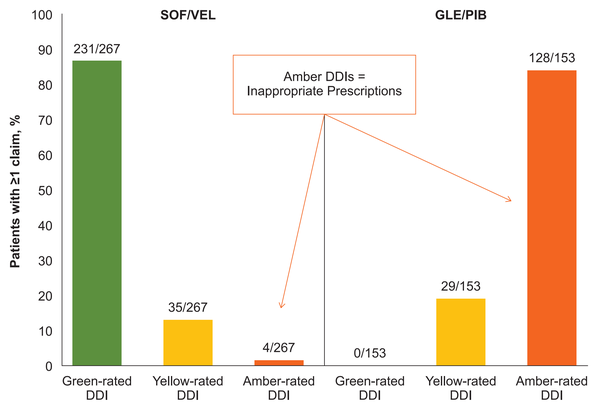
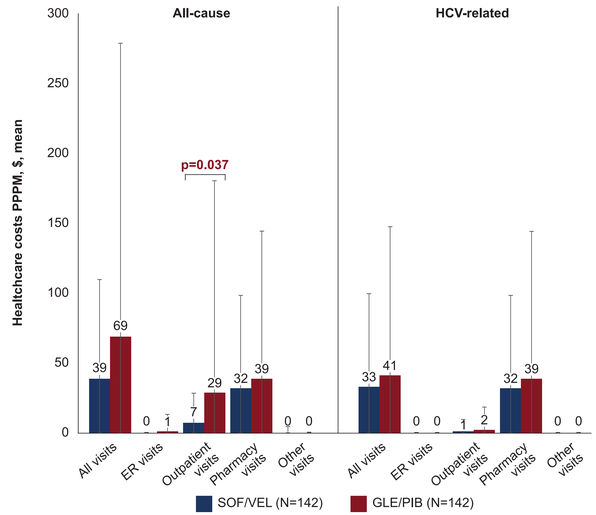
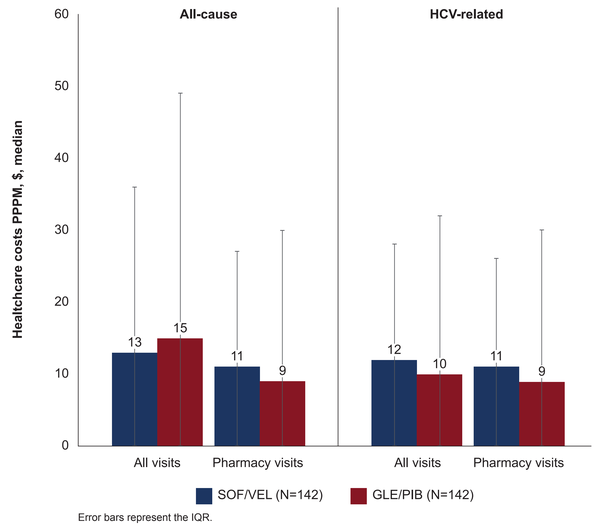


Figure 2. Mean Healthcare Costs PPPM During the 6-Month Follow-Up Period in the Propensity-Matched Cohort



Error bars indicate the SD. When the SD exceeded the mean, the lower bound was adjusted to zero.

Figure 3. Median Healthcare Costs PPPM During the 6-Month Follow-Up Period in the Propensity-Matched Cohort



Error bars represent the IQR.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ATC, Anatomical Therapeutic Chemical; CCI, Charlson Comorbidity Index; DAA, direct acting antiviral; DDI, drug-drug interaction; DDIRC, DDI-related co-medication; DDIRM, DDI-related medication; EASL, European Association for the Study of the Liver; ER, emergency room; GLE/PIB, glecaprevir/pibrentasvir; HCRU, healthcare resource use; HCV, hepatitis C virus; IQR, interquartile range; N05A, antipsychotic medications per ATC classification; PI, protease inhibitor; PPPM, per patient per month; PS, propensity score; SD, standard deviation; SOF/VEL, sofosbuvir/velpatasvir; US, United States.

References: **1.** Schaefer M, et al. J Hepatol. 2012;57(6):1379–90. doi:10.1016/j.jhep.2012.07.037. **2.** Burger D, et al. J Hepatol. 2013;58(4):792–800. doi:10.1016/j.jhep.2012.10.027. **3.** Back D, Else L. Dig Liver Dis. 2013;45(S5):S343–8. doi:10.1016/j.dld.2013.07.008. **4.** Pawlotsky JM, et al. J Hepatol. 2020;73(5):1170–1218. doi:10.1016/j.jhep.2020.08.018. **5.** Liverpool HEP Interactions. Published 2021. Accessed March 31, 2025. https://www.hep-druginteractions.org/checker. **6.** AASLD Hepatitis C Point of Care Test and Treat Algorithm. Published 2025. Accessed March 31, 2025. https://www.hcvguidelines.org/. **7.** NIPH ATC/DDD Index. Published 2024. Accessed March 31, 2025. https://atcddd.fhi.no/atc_ddd_index/?code=n05a.

Funding Details: This research and medical writing and graphic design support were funded by Gilead Sciences, Parsippany, United States.

Disclosures: **DM** and **CD** report employment with Gilead Sciences. **TD** was an employee of Smart Data analysis and Statistics, at the time this study was conducted, which received fees from Gilead Sciences for conducting this work.

Acknowledgements: The authors acknowledge Xiu Chen, previous employee of Gilead Sciences, for her work on this study. Medical writing support was provided by PJ Membrino, Costello Medical, Inc. and Nnenna Ene, Costello Medical, Inc. Graphic design support was provided by Jessica Brown, Costello Medical, Inc., funded by Gilead Sciences.