Real-World Implications of the New AASLD/IDSA HCV "Test and Treat" Algorithm: Focus on Cardiovascular Comedications in Hepatitis C Virus (HCV) Patients Receiving Direct-Acting Antivirals (DAAs)

3058

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Conclusions

- Under the AASLD/IDSA algorithm, DDIs relating to cardiovascular medications being prescribed alongside DAAs could lead to a substantial need for specialist consultation, especially when protease inhibitor (PI)-based DAAs such as GLE/PIB are selected. This represents a barrier to rapid "test and treat" implementation
- Strategic DAA selection based on individual DDI profiles could avert a notable proportion of potential specialist referrals, thereby supporting faster, simplified HCV care
- Targeted prescriber education on high-risk drug pairs (e.g., GLE/PIB with atorvastatin, simvastatin; GLE/PIB with olmesartan, prazosin) is warranted to optimize regimen choice
- Future analyses should evaluate the downstream impact of DDI-driven consultations on treatment delays, healthcare utilization, and overall HCV cure rates

Plain Language Summary

- People with hepatitis C virus (HCV) may need to receive multiple medications at the same time for their HCV as well as other conditions, such as cardiovascular (heart/blood vessel) disease. This can lead to a risk of effects between drugs called drug-drug interactions (DDIs). Before patients start treatment for HCV, guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) recommends that doctors check for potential DDIs
- Sofosbuvir/velpatasvir (SOF/VEL) and glecaprevir/pibrentasvir (GLE/PIB) are medications for treating people with HCV that work in different ways
- In this study, on average, patients receiving GLE/PIB had more severe DDIs than SOF/VEL for drugs used for high blood pressure (antihypertensives) and high cholesterol (lipid-lowering medications)
- Checking the risk of drug interactions early and giving patients medications with a lower risk of interactions may help to avoid unnecessary visits with doctors

Background

- People with hepatitis C virus (HCV) frequently need to take cardiovascular medications, such as antihypertensive or lipid-lowering medications, as they experience a higher risk of major atherosclerotic cardiovascular events versus uninfected individuals[1,2]
- This co-use can lead to a risk of drug-drug interactions (DDIs) that can impact patient safety, and increase healthcare resource utilization (HCRU)[3,4]
- The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) endorse the University of Liverpool DDI tracker (https://www.hep-druginteractions.org/) in their Hepatitis C Point of Care (POC) Test and Treat Algorithm for reconciliation of potential DDIs with concomitant medications before initiating DAA therapy. If DDIs are identified, specialist consultation is advised, potentially adding complexity to an otherwise expedited care pathway initiation[5–7]
- This study aimed to assess the real-world applicability of this POC algorithm by evaluating the impact of cardiovascular comedications, specifically antihypertensive and lipid-lowering medications, on DDI risk among US HCV patients receiving the DAAs sofosbuvir/velpatasvir (SOF/VEL) and glecaprevir/pibrentasvir (GLE/PIB)

Methods

- This retrospective cohort study identified patients treated for chronic HCV using data from 01 July 2015 to 30 June 2023 in the IQVIA PharMetrics Plus database
- Patients were included if they had a claim for SOF/VEL or GLE/PIB overlapping with a DDI-related medication (DDIRM). DDIRMs with a 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) to 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:[3]

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

- DDI risk was reconciled with the AASLD/IDSA algorithm's guidance to determine whether patients would require specialist consultation; contraindicated, clinically significant, and weak DDIs were evaluated as those requiring specialist consultation
- A DDIRC severity score was calculated for each patient using a scoring system of red (3 points), amber (2 points), and yellow (1 point) for each claim where a DDRIC was recorded
- Matched cohorts were created using 1:1 propensity score (PS) matching without replacement to compare DDI risk between SOF/VEL and GLE/PIB patients
  - PS matching accounted for age, gender, insurance status, HCV index year, weighted Charlson Comorbidity Index (CCI), and specific comorbidities (i.e., gastroesophageal reflux disease, epilepsy, and hyperlipidemia) as covariates

Results

- 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, 2.5% (280/11,324) were receiving concomitant antihypertensive medication and 11.6% (1,317/11,324) lipid-lowering medication
- After PS matching, the antihypertensive and lipid-lowering medication cohorts consisted of 182 (SOF/VEL: n=91; GLE/PIB: n=91) and 862 (SOF/VEL: n=431; GLE/PIB: n=431) patients receiving DAAs concomitantly with cardiovascular medication, respectively; all patient characteristics were broadly similar between matched SOF/VEL and GLE/PIB cohorts (**Table 1**)

Antihypertensive Medications (Matched Cohort)

- Most patients had one claim for a concomitant antihypertensive medication with potential DDI risk (98.9% [180/182]). Only 2.2% (2/91) of SOF/VEL and 0% (0/91) GLE/PIB patients had ≥2 claims for antihypertensive medications with potential DDI risk
- Among the 91 patients on SOF/VEL, none had claims for medications with weak DDI risk and 23.1% (21/91) had claims with clinically significant DDI risk. For the 91 GLE/PIB treated patients, 4.4% (4/91) had claims with weak DDI risk and 95.6% (87/91) had clinically significant DDI risk. No patients in either cohort had a claim showing contraindicated DDI risk
  - When reconciled with the AASLD/IDSA algorithm, 23.1% (21/91) SOF/VEL patients and all GLE/PIB patients would need a specialized consultation when following the recommendations regarding DDI reconciliation
- The four most common concomitant antihypertensive medications, for either SOF/VEL or GLE/PIB, were olmesartan, prazosin, enalapril, and irbesartan; For GLE/PIB, all four medications had clinically significant DDI risk. For SOF/VEL patients, only prazosin had clinically significant DDI risk (**Figure 1**)
- The DDIRC severity score (mean [SD]) was 0.46 (0.85) and 1.96 (0.21) for the SOF/VEL and GLE/PIB cohorts, respectively. The maximum DDIRC severity score was 2 in both cohorts; the majority of SOF/VEL patients had a severity score of 0 while the majority of GLE/PIB patients a score of 2 (**Figure 2**)

Lipid-Lowering Medications (Matched Cohort)

- Most patients had one claim for a concomitant lipid-lowering medication with potential DDI risk (94.1% [811/862]). Only 4.2% (18/431) and 7.7% (33/431) of SOF/VEL and GLE/PIB patients, respectively, had ≥2 claims for lipid-lowering medications with potential DDI risk
- None of the 431 patients on SOF/VEL had claims for medications with a weak DDI risk, whilst 88.2% (380/431) had claims with clinically significant DDI risk. Similarly, none of the 431 GLE/PIB treated patients had claims with a weak DDI risk, whilst 32.7% (141/431) had claims with a clinically significant DDI risk; no SOF/VEL patients had contraindicated DDI risk claims while 74.4% (321/431) of GLE/PIB patients did
  - When reconciled with the AASLD/IDSA algorithm, 85.4% (368/431) of SOF/VEL patients and all GLE/PIB patients would require specialist consultation when following the recommendations
- The four most common concomitant lipid-lowering medications, for either SOF/VEL or GLE/PIB, were atorvastatin, rosuvastatin, pravastatin, and simvastatin; of these, two drugs had contraindicated DDI risk for GLE/PIB patients. None had contraindicated DDI risk for SOF/VEL patients (**Figure 3**)
  - Regarding multi-DDI risk, 1.4% (6/431) SOF/VEL patients had 2 claims both with clinically significant DDI risk; of GLE/PIB treated patients, 1 (0.2%) had 2 claims both with clinically significant risk and 1 (0.2%) had 2 claims both with contraindicated DDI risk
- The DDIRC severity score (mean [SD]) was 1.79 (0.70) for the SOF/VEL cohort and 2.90 (0.75) for the GLE/PIB cohort. In the SOF/VEL cohort, the majority of patients had a DDIRC severity score of 2, whilst the remainder had a score of 0 or 4. In the GLE/PIB cohort, most patients had a DDIRC severity score of 3 and none had a score of 0 (**Figure 4**)

Table 1. Patient Characteristics

Characteristic		Antihypertensive Medications: Matched Cohort				Lipid-Lowering Medications: Matched Cohort			
		Overall	SOF/VEL	GLE/PIB	p-value	Overall	SOF/VEL	GLE/PIB	p-value
N		182	91	91		862	431	431	
Age at index, mean (SD)		54.25 (12.32)	54.21 (12.70)	54.30 (12.01)	0.962	59.28 (7.50)	59.29 (7.02)	59.27 (7.97)	0.967
Gender, n (%)	Male	111 (61.0)	57 (62.6)	54 (59.3)	0.761	607 (70.4)	304 (70.5)	303 (70.3)	1.000
	Female	71 (39.0)	34 (37.4)	37 (40.7)		255 (29.6)	127 (29.5)	128 (29.7)	
Insurance, n (%)	Commercial	109 (59.9)	53 (58.2)	56 (61.5)	0.766	549 (63.7)	273 (63.3)	276 (64.0)	0.932
	Medicare	10 (5.5)	5 (5.5)	5 (5.5)		81 (9.4)	39 (9.0)	42 (9.7)	
	Medicaid	1 (0.5)	1 (1.1)	0 (0.0)		5 (0.6)	3 (0.7)	2 (0.5)	
	Self-insured	62 (34.1)	32 (35.2)	30 (33.0)		227 (26.3)	116 (26.9)	111 (25.8)	
HCV index year, n (%)	2017	15 (8.2)	8 (8.8)	7 (7.7)	0.983	35 (4.1)	18 (4.2)	17 (3.9)	0.321
	2018	43 (23.6)	21 (23.1)	22 (24.2)		243 (28.2)	106 (24.6)	137 (31.8)	
	2019	50 (27.5)	25 (27.5)	25 (27.5)		248 (28.8)	130 (30.2)	118 (27.4)	
	2020	31 (17.0)	14 (15.4)	17 (18.7)		157 (18.2)	81 (18.8)	76 (17.6)	
	2021	29 (15.9)	16 (17.6)	13 (14.3)		120 (13.9)	63 (14.6)	57 (13.2)	
	2022	14 (7.7)	7 (7.7)	7 (7.7)		59 (6.8)	33 (7.7)	26 (6.0)	
CCI, weighted (mean [SD])		3.13 (1.77)	3.22 (1.78)	3.03 (1.76)	0.477	3.91 (1.92)	3.90 (1.80)	3.92 (2.03)	0.845
Gastroesophageal reflux disease, n (%)	No	139 (76.4)	68 (74.7)	71 (78.0)	0.727	666 (77.3)	334 (77.5)	332 (77.0)	0.935
	Yes	43 (23.6)	23 (25.3)	20 (22.0)		196 (22.7)	97 (22.5)	99 (23.0)	
Epilepsy, n (%)	No	181 (99.5)	90 (98.9)	91 (100.0)	1.000	851 (98.7)	426 (98.8)	425 (98.6)	1.000
	Yes	1 (0.5)	1 (1.1)	0 (0.0)		11 (1.3)	5 (1.2)	6 (1.4)	
Hyperlipidemia, n (%)	No	115 (63.2)	54 (59.3)	61 (67.0)	0.356	225 (26.1)	108 (25.1)	117 (27.1)	0.535
	Yes	67 (36.8)	37 (40.7)	30 (33.0)		637 (73.9)	323 (74.9)	314 (72.9)	

Figure 1. Concomitant Use of HCV Treatment and DDIRM by Medication and DDI Risk Level: Antihypertensive Medications (Matched Cohort)

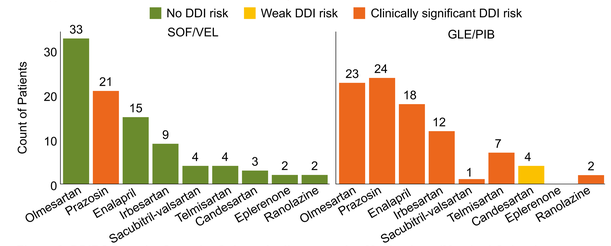


Figure 2. DDIRC Severity Score by Cohort: Antihypertensive Medications (Matched Cohort)

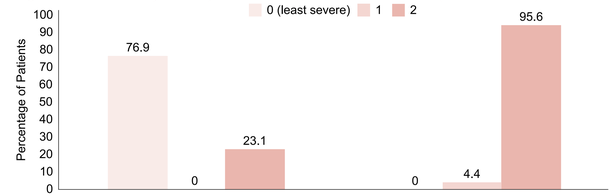


Figure 3. Concomitant Use of HCV Treatment and DDIRM by Medication and DDI Risk Level: Lipid-Lowering Medications (Matched Cohort)

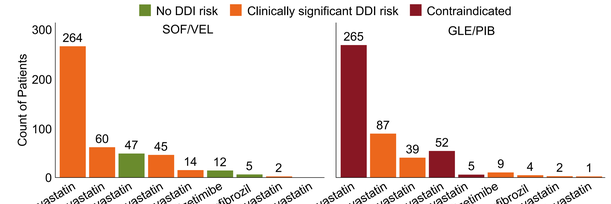
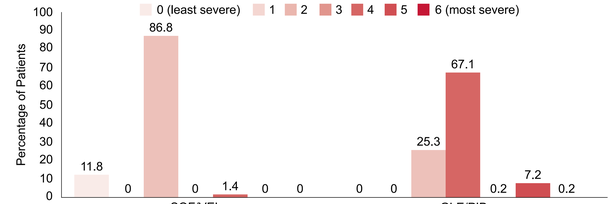


Figure 4. DDIRC Severity Score by Cohort: Lipid-Lowering Medications (Matched Cohort)



Abbreviations: CCI, Charlson Comorbidity Index; DAA, direct acting antiviral; DDI, drug-drug interactions; DDIRC, drug-drug interaction-related comedication; DDIRM, drug-drug interaction-related medication; GLE/PIB, glecaprevir/pibrentasvir; HCV, hepatitis C virus; HCRU, healthcare resource utilization; IDSA, Infectious Diseases Society of America; PI, protease inhibitor; POC, point of care; SD, standard deviation; SOF/VEL, sofosbuvir/velpatasvir; US, United States.

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