Evaluating utilization and management of comedications with potential for drug-drug interactions among patients with chronic hepatitis C initiating treatment with sofosbuvir/velpatasvir or glecaprevir/pibrentasvir

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Key Findings

In this sample of patients initiating therapy with direct acting antiviral agents (DAAs) for the treatment of chronic hepatitis C (HCV), a greater proportion of GLE/PIB initiators had any drug interaction (DDI) comedication use compared to SOF/VEL initiators (66.8% vs 43.7%, p <0.01); DDI comedication use decreased during DAA treatment but remained higher in patients initiating GLE/PIB than patients initiating SOF/VEL (41.5% vs 28.9%, p < 0.01) (Figure 1)

After adjusting for other factors, GLE/PIB initiators had higher odds of having any DDI-related comedication use in the follow-up period compared to SOF/VEL initiators; factors such as age, baseline comorbidities and all cause healthcare resource utilization were associated with greater odds of having any DDI-related comedication use in the follow-up period (Figure 2)

Compared with patients on SOF/VEL, patients on GLE/PIB were more likely to discontinue their DDI-related comedication upon initiation of DAA therapy (Figure 3)

Compared with patients on SOF/VEL, patients on GLE/PIB were more likely to decrease their DDI-related comedication dose or switch to a non-DDI-related comedication after starting DAA therapy (Figure 4)

Conclusions

DDI-related comedication use was identified among a substantial proportion of patients initiating DAA therapy, with higher rates of use observed among patients initiating GLE/PIB than those initiating SOF/VEL

Among patients with baseline DDI-related comedication use, those initiating GLE/PIB were more likely to discontinue their DDI-related comedication prior to DAA initiation than patients initiating SOF/VEL

In patients who continued DDI-related comedication while on their index DAA therapy, patients initiating GLE/PIB had higher rates of dose decrease and switches to non-DDI-related comedications than those initiating SOF/VEL

Results from this study as well as future studies evaluating the real-world impact of potential DDIs may help to optimize treatment decisions and decrease healthcare resource utilization (HCRU) and costs for patients treated for HCV

References: 1. AASLD/IDSA HCV Guidance Panel. HCV guidance: recommendations for testing, managing, and treating hepatitis C. Updated October 24, 2022. https://www.hcvguidelines.org/sites/default/files/full-guidance-pdf/AASLD-IDSA_HCVGuidance_October_24_2022.pdf. Accessed February 23, 2023. 2. University of Liverpool. Hepatitis drug interaction database. www.hep-druginteractions.org. Accessed February 23, 2023.

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Introduction

- Guidelines recommend that nearly all individuals with HCV infection receive treatment with DAA agents[1]
- Because of the potential DDIs it is recommended that clinicians assess potential DDI risk prior to initiating DAA therapy[1]
- Two pan genotypic DAA regimens:
  - Glecaprevir/pibrentasvir (GLE/PIB) – a protease inhibitor with known drug-drug interaction (DDI) effects
  - Sofobuvir/velpatasvir (SOF/VEL) – a protease inhibitor-free regimen with a more favorable DDI profile

Objective

- To compare rates and management of comedications with DDI risk (DDI comedications) among patients initiating DAA treatment with SOF/VEL or GLE/PIB

Methods

- **Study design:** retrospective observational analysis using administrative claims from the Optum Research Database
  - Study population: adults with ≥ 1 pharmacy claim for SOF/VEL or GLE/PIB from July 2016 to April 2020 (index date = date of first claim)
  - Continuous enrollment 12 months before (baseline) and 6 months after the index date (follow-up)
  - ≥ 1 diagnosis for HCV during the baseline period or on the index data
  - Patients were excluded if they had liver disease or HCV treatment at baseline, or hepatitis B or HIV during the study period
- **Study variables:**
  - Baseline patient characteristics: demographic information, comorbid conditions, all-cause healthcare resource utilization
  - DDI-related comedication use and risk levels (category 3 – do not co-administer, category 2 – potential interaction, category 1 – potential weak interaction) [2]
    - Select DDI-related comedications – the 12 most prevalent DDI-related comedications
  - DDI-related comedication actions (measured among patients with ≥ 1 DDI-related comedication during the 90-days before index): discontinuation, dose decrease, change to non-DDI-related medication
- **Analysis**
  - All variables were analyzed descriptively and stratified by index DAA therapy
  - Between-cohort differences in patient characteristics were evaluated using chi square tests and two-sample t-tests
  - The association between index DAA therapy and DDI-related comedication use in follow-up was assessed with logistic regression

Results

- A total of 4,528 patients were included in the study population; 2,351 initiated SOF/VEL and 2,177 initiated GLE/PIB; the overall population was 60.6% male with a mean age of 59.2 years (**Table 1**)
- DDI-related comedication use:
  - Compared to SOF/VEL initiators, GLE/PIB initiators had higher baseline rates of category 3 (21.4% vs 2.3%), category 2 (51.9% vs 41.6%), and category 1 (31.4% vs 2.8%, all p < 0.001) DDI-related comedications (**Figure 1**)
  - DDI-related comedication use decreased during DAA treatment but remained higher in GLE/PIB initiators vs SOF/VEL initiators (41.5% vs 28.9%, p < 0.001) (**Figure 1**)

Results cont.

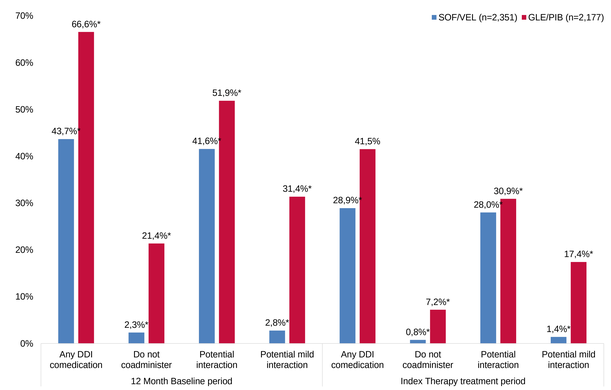
- Adjusting for baseline covariates, GLE/PIB vs SOF/VEL initiators had 1.8 and 10.2 times the odds of any DDI-related comedication use in the follow-up period, (p < 0.001) (**Figure 2**)
- Select DDI-related comedication actions
  - A total of 1,637 patients had ≥ 1 pharmacy fill for a select DDI-related comedication in the 90 days prior to index (**Figure 3**)
  - A higher proportion of GLE/PIB vs SOF/VEL initiators discontinued ≥ 1 DDI-related comedication before initiating DAA treatment (52.2% vs 38.0%, p < 0.001) (**Figure 3**)
  - GLE/PIB vs SOF/VEL initiators had higher rates of dose decrease (10.8% vs 6.8%, p = 0.026) and change to medication with no DDI risk (3.5% vs 1.1%, p = 0.014) (**Figure 4**)

Table 1. Overall patient demographic and clinical characteristics

	Total n = 4,528	SOF/VEL n = 2,351	GLE/PIB n = 2,177	p-value
Age, mean (SD)	59.2 (12.3)	59.4 (12.1)	58.9 (12.5)	0.170
Male gender, n (%)	2,743 (60.6)	1,442 (61.3)	1,301 (59.8)	0.279
Insurance type, n (%)				
Commercial	2,127 (47.0)	1,120 (47.6)	1,007 (46.3)	0.352
Medicare	2,401 (53.0)	1,231 (52.4)	1,170 (53.7)	0.352
Quan-Charlson comorbidity index score, mean (SD)	2.7 (1.4)	2.7 (1.4)	2.8 (1.5)	0.078
Liver disease severity, n (%)				
No cirrhosis	4,222 (93.2)	2,155 (91.7)	2,067 (95.0)	<0.001
Compensated cirrhosis	306 (6.8)	196 (8.3)	110 (5.1)	<0.001
Baseline conditions, n (%)				
Heart disease[1]	1,310 (28.9)	634 (27.0)	676 (31.1)	0.002
Obesity/overweight	1,478 (32.6)	723 (30.8)	755 (34.7)	0.005
Tobacco use	1,644 (36.8)	813 (34.6)	851 (39.1)	0.002
Renal insufficiency[2]	888 (19.6)	413 (17.6)	475 (21.8)	<0.001
Baseline AHRQ comorbidities, n (%)				
Other nutritional, endocrine, metabolic disorders	2,001 (44.2)	982 (41.8)	1,019 (46.8)	<0.001
Other nervous system disorders	1,530 (33.8)	753 (32.0)	777 (35.7)	0.009
Upper gastrointestinal disorders	556 (51.4)	221 (49.1)	335 (53.1)	0.197
All-cause healthcare resource utilization, mean (SD)				
Ambulatory visits	23.9 (27.4)	21.9 (20.4)	26.1 (33.3)	<0.001
Inpatient stay	0.2 (0.6)	0.2 (0.5)	0.2 (0.7)	0.031
Pharmacy fills	30.9 (31.5)	30.0 (30.4)	31.9 (32.7)	0.043

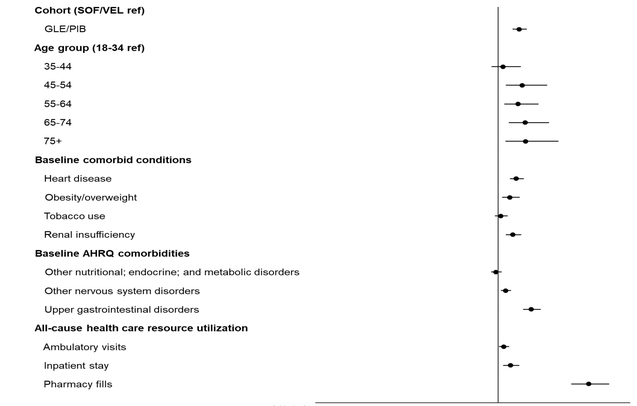
[1]Includes diagnoses for acute myocardial infarction, dysrhythmia, ischemic heart disease, heart failure, or peripheral vascular disease
[2]Includes diagnoses for chronic kidney disease and end-stage renal disease
AHRQ, Agency for Healthcare Research and Quality; GLE/PIB, glecaprevir/pibrentasvir; SOF/VEL, sofosbuvir/velpatasvir

Figure 1. DDI-related comedication use by risk level



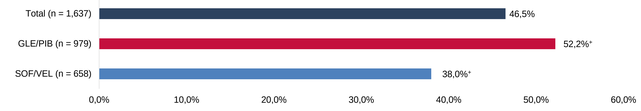
*p < 0.001 in comparison between patients initiating SOF/VEL versus GLE/PIB; GLE/PIB, glecaprevir/pibrentasvir; SOF/VEL sofosbuvir/velpatasvir

Figure 2. Association between index DAA therapy and any DDI-related comedication use in the follow-up period



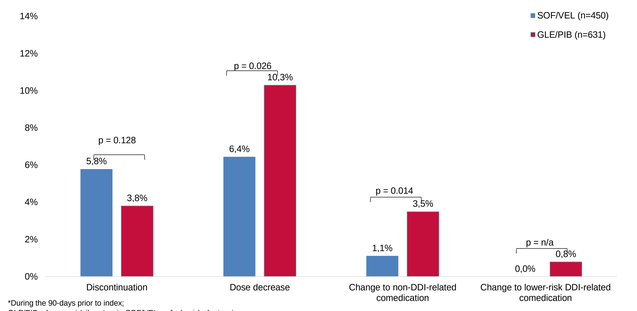
The following variables were included from the model but were not presented in the visualization: index year, baseline compensated cirrhosis, anemia, immunizations and screenings for infection disease, liver disease, substance-related disorders, disease of the urinary system;
GLE/PIB, glecaprevir/pibrentasvir; SOF/VEL, sofosbuvir/velpatasvir

Figure 3. DDI-related comedication discontinuation at index among patients with ≥ 1 select DDI-related comedication*



* During the 90 days prior to index
* p < 0.001 in comparison between patients initiating SOF/VEL versus GLE/PIB
GLE/PIB, glecaprevir/pibrentasvir; SOF/VEL, sofosbuvir/velpatasvir

Figure 4. Actions during index DAA therapy among patients with ≥ 1 select DDI-related comedication*



*During the 90-days prior to index;
GLE/PIB, glecaprevir/pibrentasvir; SOF/VEL, sofosbuvir/velpatasvir

Limitations

- Medication use was measured from pharmacy claims; patients may not have utilized medications as prescribed
- Adverse events are underreported in claims data and were not captured in this study
- This study was conducted in a large US managed care population, results may not be representative of all patients with HCV initiated on SOF/VEL or GLE/PIB