Use of proton pump inhibitors among German Hepatitis C patients treated with sofosbuvir/velpatasvir: Data from the German Hepatitis C-Registry (2016 - 2022)

Poster #THU-366

Viral Hepatitis

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Conclusions

- PPI co-use did not impact the SVR (= 96%) in patients under SOF/VEL therapy in the DHC-R
- Comparatively high cure rates were found in SOF/VEL users irrespective of PPI co-use (SVR = 96% - 100%) in a variety of subpopulations (all genotypes with or without CC) further supporting the effectiveness of SOF/VEL in wide population groups
- No negative PPI dose-dependent SVR trend was seen; co-use of metamizole did not impact the SVR (= 100%) supporting the effectiveness in a multi-drug-drug interaction scenario
- The present data support the use of SOF/VEL according to labeled recommendations with respect to co-administration of PPIs and other acid reducing agents[1]

Plain Language Summary

- The German Hepatitis C-Registry (DHC-R) is an ongoing registry collecting information on patients with a hepatitis C virus (HCV) infection; it includes about 18,900 patients
- We studied the use of drugs which reduce the stomach acid amount (PPIs) in 1,154 patients taking SOF/VEL to treat their HCV for the first time
- The number of patients cured of HCV [assessed 12 weeks after end of treatment (SVR)] was similarly high (≥ 96%) between patients taking PPIs and those who did not, regardless of their genotype or whether they had compensated cirrhosis. Co-use of metamizole with PPIs also had no impact on the cure rate (= 100%)

References: **1**. SmPC Epclusa®; August 2023. **2**. Rumph DM, et al. Pharmacotherapy. 2022;42(5):397-404. **3.** University of Liverpool. Hep drug interactions. Available at: https://www.hep-druginteractions.org/ (accessed April 2024). **4**. Tacke F, et al. *EASL.* 2022;Poster #FRI393.

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Introduction and objectives

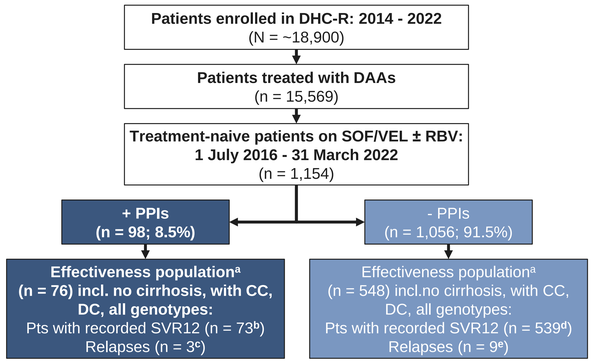
- Literature[2] and product label[1] suggest velpatasvir bioavailability may be reduced when administered concomitantly with a proton pump inhibitor (PPI) based on pharmacokinetic studies
- The German Hepatitis C-Registry (Deutsches Hepatitis C-Register, DHC-R) is a national, ongoing, noninterventional, prospective, observational, multicenter real-world registry including ~ 18,900 patients
- We aimed to retrospectively determine the clinical relationship between PPI use and sustained virologic response rates (SVR) in patients taking sofosbuvir/velpatasvir (SOF/VEL) ± ribavirin (RBV) in the DHC-R

Methods

- The present analysis is based on 1,154 patients treated with SOF/VEL ± RBV, enrolled in the DHC-R between 2016 and 2022
  - This population was split between patients with / without PPI co-use
- Analysis included baseline characteristics and SVR (patients with SVR available), based on modified intention to treat (mITT), including patients with ITT SVR (SVR at week 12) and ITT relapses
  - PPI co-use with direct acting antivirals (DAA), poses the risk drug-drug interactions (DDI); as metamizole shows the same risk of DDIs as PPIs,[3] thus checking a multi-DDI scenario[4]

Results

Figure 1. Patient flow chart



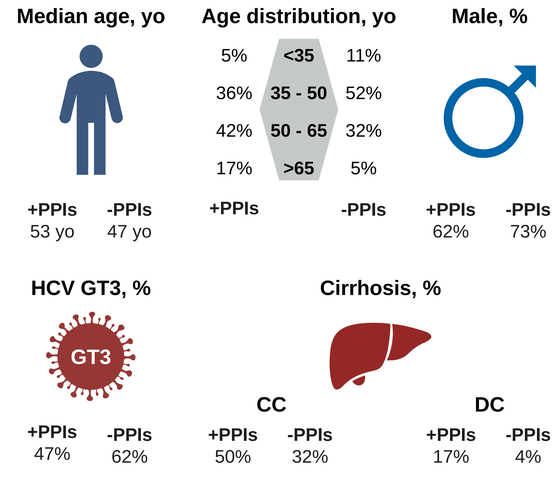
[a]mITT was used to assess therapy effectiveness including patients with SVR12 data available, while excluding patients with missing SVR data, therapy discontinuation, non-response EoT, and confirmed and possible reinfections.
[d]Thereof SOF/VEL + RBV: n = 32 ([e]1 relapse). [b]Thereof SOF/VEL + RBV: n = 6 ([c]0 relapses).
CC, compensated cirrhosis; DAA, direct antiviral agents; DC, decompensated cirrhosis; DHC-R, German Hepatitis C-Registry (Deutsches Hepatitis C-Register); EoT, end of treatment; mITT, modified intention to treat analysis; n, number; PPI, proton pump inhibitor; Pts, patients; RBV, ribavirin; SOF/VEL, sofosbuvir/velpatasvir; SVR12, sustained virologic response rate in week 12.

Disclosures: **MC** received honoraria for lectures and / or consulting from Abbvie, AiCuris, Dr. Falk Pharma GmbH, Gilead Sciences, Inc., GSK, MSD Sharp & Dohme, and Roche. **GT** served as speaker for Abbvie, Advanz Pharma, and Gilead Sciences, Inc.; provided consultancy for Gilead Sciences, Inc. **UN** served as speaker for Abbvie, Camurus, Gilead Sciences, Inc., and VIIV Healthcare; and participated in advisory boards for Abbvie, Camurus, Gilead Sciences, Inc., and VIIV Healthcare. **AS, RL, HK, and CJ** have nothing to disclose. **CH, and MS** are employees of Gilead and own equity in Gilead Sciences, Inc. **CS** served as speaker for Abbvie and Gilead Sciences, Inc.; and participated in advisory boards for Abbvie and Gilead Sciences, Inc.

Results

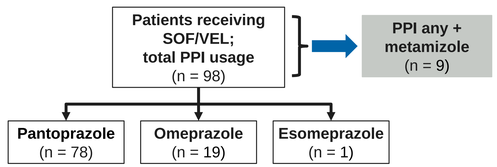
- PPI co-users were older, with more females, less genotype 3 (GT3), but with more compensated cirrhosis (CC) and decompensated cirrhosis (DC) (**Figure 2**)

Figure 2. Demographics



Data presented as median years and %.
CC, compensated cirrhosis; DC, decompensated cirrhosis; GT3, genotype 3; n, number; PPI, proton pump inhibitor; yo, years of age.

Figure 3. Comedication of patients on SOF/VEL ± PPI ± metamizole



Data presented as n.
n, number; PPI, proton pump inhibitor; SOF/VEL, sofosbuvir/velpatasvir.

- Pantoprazole was by far the most used PPI. Metamizole co-use in the SOF/VEL + PPI group was 9.2% (**Figure 3**) and did not impact the SVR mITT in PPI users (=100%)

DHC-R Deutsches Hepatitis C-Register — Leberstiftungs GmbH

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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Management Board: Thomas Berg, Peter Buggisch, Markus Cornberg, Dietrich Hüppe, Stefan Mauss, Christoph Sarrazin, Heiner Wedemeyer.

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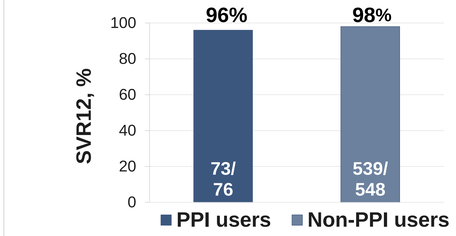
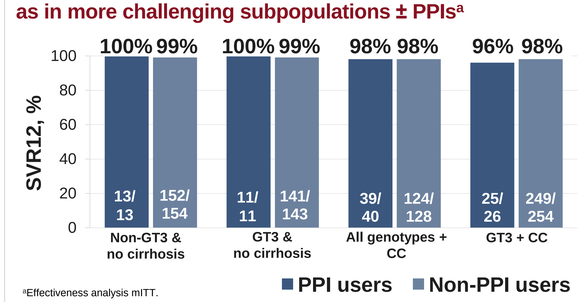
- High SVR in PPI co-use including different doses, all genotypes ± CC, DC (**Figure 4**)

Figure 4. Overall SVR high in patients with SOF/VEL ± RBV and comparable between PPI-users and non-PPI users[a]



[a]Effectiveness analysis mITT.

Figure 5. Comparatively high SVRs in easier to treat as well as in more challenging subpopulations ± PPIs[a]



[a]Effectiveness analysis mITT.

- The number of patients with a PPI dose > 20 mg for the effectiveness analysis was small; nevertheless, no negative PPI dose dependent effect on the SVR was seen. A small number of relapses (n = 3) occurred in challenging GT3 cirrhotic subgroups [+ CC (n = 1; pantoprazole 20 mg), + DC (n = 2; pantoprazole 40 mg)] (**Table 1**)

Table 1. Effectiveness in different PPI doses

PPI dose, mg	N[a]	%	Total relapse, n	Total SVR mITT, %[a]
20[b]	42	43	1	97
40[c]	31	32	2	92
80[d]	3	3	0	100
Unknown[e]	22	22	0	100
Total	98	100	3	96

[a] Effectiveness analysis mITT: 20 mg PPIs: 36/37 = 97% (1 relapse); 40 mg PPIs: 22/24 = 92% (2 relapses); 80 mg PPIs: 2/2 = 100% (0 relapses); unknown PPI doses: 13/13 = 100% (0 relapses).
[b]20 mg: pantoprazole (N = 28), omeprazole (N = 14). [c]40 mg: pantoprazole (N = 29), omeprazole (N = 2). [d]80 mg: pantoprazole (N = 2), esomeprazole (N = 1). [e]Unknown: pantoprazole (N = 19), omeprazole (N = 3).