Concomitant use of Proton Pump Inhibitors and Sofosbuvir/Velpatasvir: Evidence from Randomized Clinical Trials and Real-World Data

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Study name

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Key Findings

— **Co-use of PPI with Direct Acting Agents (DAA), such as SOF/VEL, has been reported during clinical development and clinical practice**

— **Overall SVR12 in PPI users was comparable to the reported by non-PPI users: 97% in RCTs and 99% in RWD, including GT3 and cirrhotic patients**

Conclusions

In RCTs and RWD, the single-tablet regimen of SOF/VEL for 12 weeks was effective in patients with concomitant PPI use

These data support the use of SOF/VEL according to labeled recommendations with respect to co-administration of PPIs and other acid reducing agents

Risk of DDIs linked to PPI and DAA co-use is largely manageable

Abbreviatures: PPI (Proton Pump Inhibitors), RCT (Randomized Clinical Trial), RWD (Real World Data), GT3 (genotype 3), DDIs (Drug-drug interactions)

References: 1. Mangia A, et al. Liver Int 2020;40(8):1841-52. **2.** Esteban R, et al. AASLD 2018; P702.

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Introduction

— Literature and product labels suggest velpatasvir bioavailability may be reduced when administered concomitantly with a proton pump inhibitor (PPI), based mainly on pharmacokinetic studies.

Objective

— We aimed to determine the clinical relationship between PPI use and sustained virologic response rates (SVR) in patients treated with sofosbuvir/velpatasvir (SOF/VEL) for chronic hepatitis C virus (HCV) infection in available data coming from Phase 2/3 clinical trials (RCT) and Real-Word Data (RWD).

Methods

— Retrospective and descriptive analysis of data from patients treated with SOF/VEL for 12 weeks with and without concomitant use of PPIs and participating in Phase 2/3 RCTs and RWD studies. In RCT, PPI use was captured as part of standard concomitant medication reporting, with specific details regarding PPI dosing not collected. Main variables collected for this analysis consisted of SVR12 and relapse rate. Regarding patient inclusion/exclusion criteria, please refer to References.

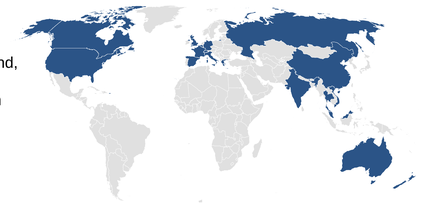
Figure 1. Data source

RCT

12 Phase 2/3 clinical trials across Australia, Belgium, Canada, China, France, Germany, Hong Kong, India, Italy, Malaysia, New Zealand, Puerto Rico, Russia, Singapore, Spain, Switzerland, Thailand, UK, USA, and Vietnam

RWD

Integrated analysis of 12 clinical practice cohorts across Canada, France, Germany, Greece, Italy, Spain and the USA



Results

Figure 2. Patients and distribution

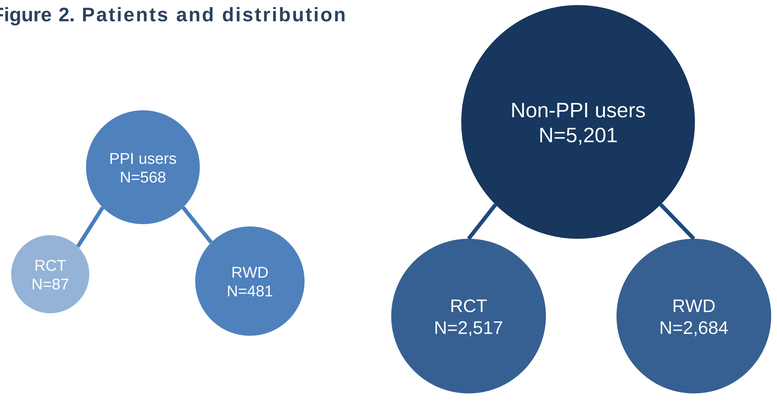
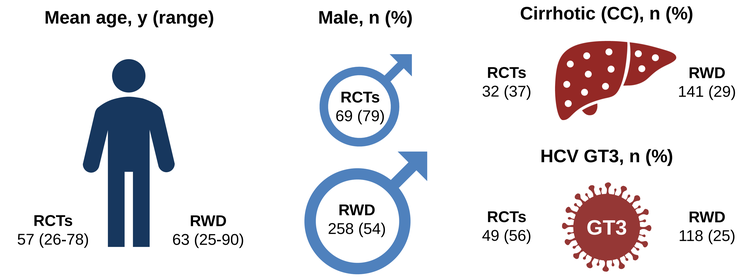
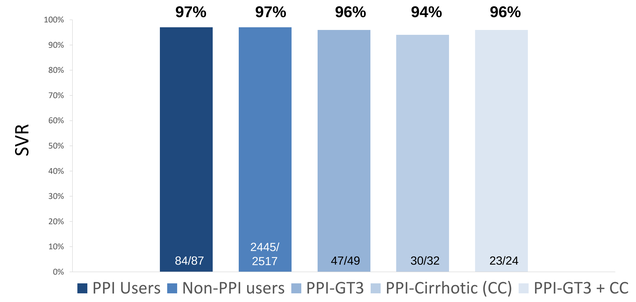


Figure 3. Demographics



— Most patients participating in RCT (66%, 57/87) continuously used PPI during the 12-week course of treatment with SOF/VEL, omeprazole being the most used PPI (68%).

Figure 4. RCT

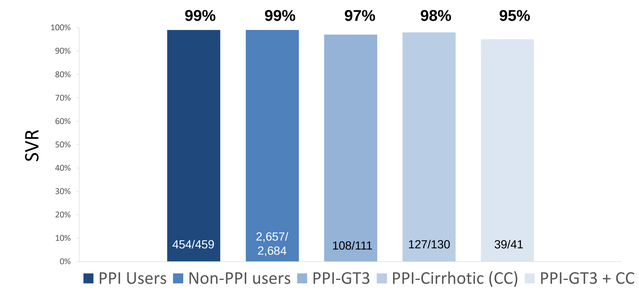


In RCT, overall SVR12 in PPI users was 97% (84/87), comparable to the reported by non-PPI users (97%).

For PPI users, SVR12 in GT3 patients was 96% (47/49), in cirrhotic (CC) was 94% (30/32). In GT3 plus CC patients, SVR12 was 96% (23/24).

— Of the 3 patients who did not achieve SVR12 in PPI-users, 2 patients relapsed (relapse rate 2%) and one patient with a history of diabetes discontinued SOF/VEL after 7 days of dosing due to hyperglycemia.

Figure 5. RWD



In RWD, overall SVR12 in PPI users was 99% (454/459), comparable to the reported by non-PPI users (99%).

For PPI users, SVR12 in GT3 was 97% (108/111) and in CC patients 98% (127/130), being of 95% (39/41) in GT3 plus CC.