Sofosbuvir/ Velpatasvir/ Voxilaprevir for DAA-experienced HCV Patients: A Systematic Review and Meta-Analysis

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ABSTRACT

Background and Aims: About 5% of chronic hepatitis-C virus (HCV) patients treated with direct-acting antivirals do not achieve sustained virological response (SVR12). We performed a systematic review and meta-analysis to evaluate the efficacy and safety of Sofosbuvir/Velpatasvir/Voxilaprevir (SOF/VEL/VOX) as salvage treatment in direct-acting antiviral (DAA)-experienced HCV patients.

Method: Search of major databases were performed from inception to 31st January 2023. Our study outcomes were SVR12 and treatment-related adverse effects. We performed subgroup analysis based on genotype, status of cirrhosis, HCC, prior SOF/VEL exposure and region. Standard meta-analysis methods were employed using the random-effects model.

Results: 24 studies (n=2,887) were included in analysis. All studies had low to moderate risk of bias. 17.2% receive SOF/VEL prior to SOV/VEL/VOX; 25% received ribavirin with SOF/VEL/VOX. 42% had pre-treatment RAS testing performed, where mutation was present in 51%,

Overall pooled SVR12 was 95.0% (95%CI: 94.0-95.8%), with lower SVR12 in real-world studies than clinical trials. Predictors for SOF/VEL/VOX failure were genotype 3 (OR 0.39, 95%CI: 0.23-0.64, I^2=7%), active HCC (OR 0.22, 95%CI: 0.08-0.57, I^2=0%) and baseline cirrhosis (OR 0.28, 95%CI: 0.13-0.57, I^2=0%), decompensated cirrhosis (OR 0.09, 95%CI: 0.03-0.23, I^2=3%) and prior SOF/VEL (OR 0.35, 95%CI: 0.13-0.94, I^2=54%). Baseline RAS mutation and ribavirin supplementation in SOF/VEL/VOX therapy were not associated with higher SVR12. Treatment discontinuation due to drug-related problems was uncommon (10 studies, 0.2%).

Conclusion: SOF/VEL/VOX is efficacious and safe for retreatment in HCV patients with prior DAA failure, even with RAS mutation. Our findings support SOF/VEL/VOX as 1st-line rescue treatment for DAA-experienced HCV patients.

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INTRODUCTION

- Despite highly effective direct-acting antiviral drugs (DAAs), up to 5% of HCV patients fail to achieve sustained virological response at week 12 (SVR12).
- Retreatment can be challenging due to the emergence of resistance-associated substitution (RAS).
- Current guidelines recommend Sofosbuvir/Velpatasvir/Voxilaprevir (SOF/VEL/VOX) as salvage treatment for DAA-experienced HCV patients who failed to achieve SVR12.
- Global data on the practice and predictor of treatment failure of SOF/VEL/VOX among DAA-experienced HCV patients were sparse, especially in Asia and Africa.

AIM

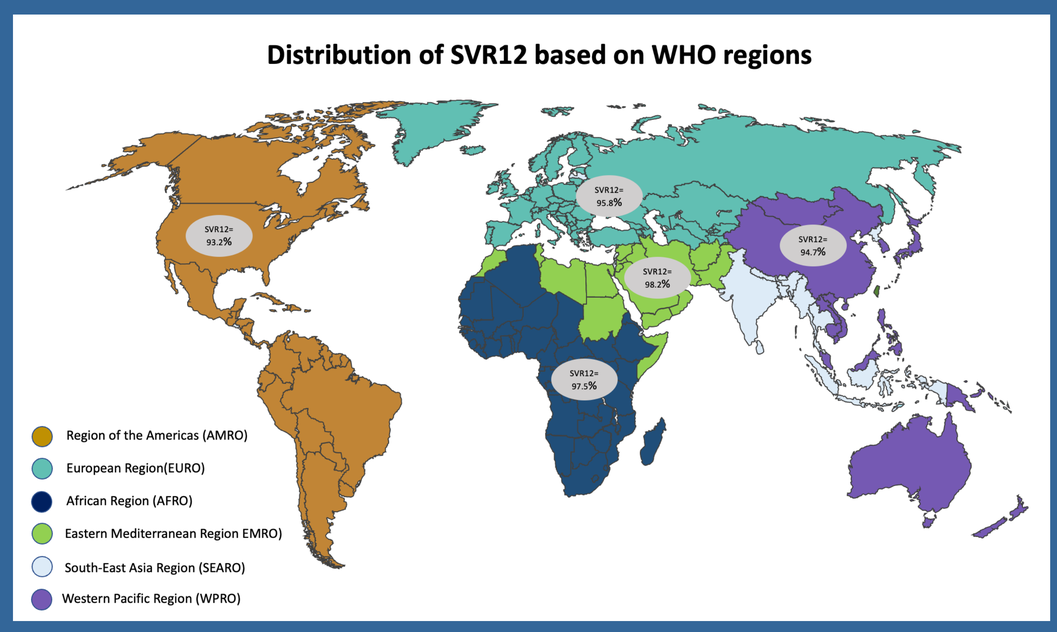
- To evaluate the efficacy and safety of SOF/VEL/VOX as salvage treatment in DAA- experienced HCV patient

METHODS

- Searched five electronic databases (PubMed, EMBASE, Cochrane Library, ClinicalTrials.gov, & Web of Science)
- Data extracted: Demographic of study participants (age and genotype of hepatitis C virus), location, sample size, RAS testing at baseline, SVR12, concurrent use of ribavirin (RBV), and treatment-related adverse events requiring discontinuation of treatment.
- Outcomes: SVR12 (both PP and ITT), treatment-related adverse events

RESULTS

- A total of 2,887 DAA- experienced HCV patients from 24 studies were reviewed
- The cohort was predominantly male (81.0%) with a diverse HCV genotype distribution (GT1 61.4%, GT2 8.2%, GT3 21.5%, GT4 7.0%, GT6 1.2%, and indeterminate GT 0.7%).
- The overall SVR12 based on PP and ITT analysis was 95% (95%CI: 94.0%-95.8%) and 88% (95%CI: 86.7%-89.5%), respectively.
- Baseline RAS mutation and ribavirin supplementation were not associated with higher SVR12
- The pooled risk of severe adverse events that occurred during SOF/VEL/VOX treatment was 1.94% (95%CI: 1.2%-2.8%).



Predictors of SVR12	Number of subjects	Odds Ratio (95% CI)	p-value
Genotype 3	1486	0.39, [0.23, 0.64]	0.37
Cirrhosis	811	0.28, [0.13,0.57]	0.68
Decompensated Cirrhosis	610	0.09, [0.03,0.23]	0.39
SOF/VEL experienced	1039	0.35, [0.13,0.95]	0.07
HCC	567	0.22, [0.09, 0.55]	0.78
RAS mutation	162	0.73, [0.11, 4.77]	0.22
Use of Ribavirin	577	0.76, [0.12, 4.68]	0.11

DISCUSSION

- **Strengths:**
  - Global perspective on effectiveness and safety of SOF/VEL/VOX.
  - Comprehensive coverage of data including Western, Asian, and African regions.
- **Limitations:**
  - Most studies did not report compliance and potential drug interaction among patients receiving SOF/VEL/VOX

CONCLUSION

- SOF/VEL/VOC is a well-tolerated and highly effective rescue therapy among DAA-experienced HCV patients Predictors of treatment failure include GT3, liver cirrhosis and active HCC