Safety and efficacy of sofosbuvir-based medication regimens with and without ribavirin in hepatitis C patients: A systematic review and meta-analysis

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Abstract

What Is Known and Objective: Sofosbuvir (SOF) is a new and highly effective medication that dramatically improved hepatitis C virus (HCV) management. However, ribavirin (RBV) is still added to SOF-based medication regimens in several clinical scenarios, despite its well-known toxicities. The aim of our study is to systematically review and analyse the impact of adding RBV to SOF-based medication regimens on clinical outcomes among HCV patients.

Methods: Included studies were randomized trials comparing the same SOF-based medication regimens with and without RBV in HCV patients and measuring serious adverse events (SAEs) and/or sustained virologic response at 12 weeks post-treatment (SVR-12). Two investigators independently searched PubMed and Cochrane Library through September 2021. The Cochrane Risk of Bias tool was used to assess trials quality. Clinical outcomes were analysed as risk ratios (RR) using a random effects model using R version 4.1.2.

Results and Discussion: Our study included a total of 26 trials with 5058 HCV patients. Quality assessment showed moderate risk of bias for most trials. Upon adding RBV, there was no significant difference in SAEs (RR 1.07, 95% CI: 0.77–1.48, I² = 10%), nor an impact on SVR-12 (RR 1.00, 95% CI: 0.98–1.01, I² = 41%). There was no evidence of publication bias for either outcome. Subgroup analysis consistently showed lack of benefit among HCV subgroups. Additionally, NCT01826981 was identified as the main source of heterogeneity in the SVR-12 outcome.

What Is New and Conclusion: Our findings suggest nonsignificant differences in safety and efficacy between SOF-based medication regimens with and without RBV which should be considered in clinical practice.

KEYWORDS
HCV patients, ribavirin, serious adverse events, sofosbuvir, sustained virologic response
1 | WHAT IS KNOWN AND OBJECTIVE

Hepatitis C virus (HCV) infection is a serious public health problem with over 71 million infections worldwide in 2015\(^1\) and 2.4 million infected adults in the United States (U.S.) alone between 2013 and 2016.\(^2\) HCV infection can frequently lead to the development of cirrhosis and/or liver cancer in the long-term and increases the risk of death among infected patients.\(^3\) In the U.S., HCV-related liver damage is the leading cause of the subsequent liver transplantation.\(^4\)

Previously, a limited number of antiviral therapies were available for HCV treatment including interferon (INF) and ribavirin (RBV).\(^5\) However, those therapies were of low benefit and had a significant rate of side effects.\(^6\) Recently, the development of new direct-acting antivirals (DAAs) introduced a substantial improvement in HCV management.\(^7\) This class prevents virus replication and demonstrates a higher cure rate, fewer adverse events, and better tolerability relative to the previous treatments.\(^7\) Importantly, the recent cohort study by Kalidindi and colleagues revealed an association between treatment with DAAs and reduction in overall mortality rates.\(^8\)

Among the new and most effective DAAs, sofosbuvir (SOF) has been recommended by the World Health Organization (WHO) as an essential medicine for HCV treatment.\(^7\) Sofosbuvir is an oral antiviral with high efficacy (cure rate exceeds 90%), potency against all HCV genotypes (GTs), improved safety profile, and a simple dosing regimen.\(^10\) Sovaldi (SOF alone, Gilead Sciences, USA) was the first SOF medication approved by the Food and Drug Administration (FDA) in 2013 to be used in combination with other antivirals for adults with HCV.\(^11\) Later, the FDA approved several DAAs for the same manufacturer as combinations with SOF including Harvoni (SOF + LDV/ledipasvir), Eclusa (SOF + VEL/velpatasvir) and Vosevi (SOF + VEL + VOX/voxilaprevir).\(^12\) However, SOF-based medication regimens are one of the most expensive medications in the U.S.\(^13\) A tablet of Sovaldi costs $1000 and $1125 for Harvoni, resulting in a 3-month course regimen costing more than $80,000.

Despite SOF-based medication regimens merit and RBV’s well-known toxicities, the current national and international guidelines\(^14,15\) still recommend the addition of RBV to SOF-based medication regimens in specific clinical scenarios, especially in patients who failed initial treatment. The aim of our study is to systematically review the currently available evidence in randomized trials and analyse the impact of adding RBV to SOF-based medication regimens on clinical outcomes among a diverse HCV patient profile.

2 | METHODS

2.1 | Overview

This study is a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) compliant systematic review and meta-analysis comparing SOF-based medication regimens with and without RBV for the primary clinical outcomes of the rate of serious adverse events (SAEs) and successful sustained virologic response at 12 weeks post-treatment (SVR-12) among HCV patients.

2.2 | Search strategy

Included studies were randomized clinical trials (RCTs) comparing the same SOF-based medication regimens with and without RBV in adults with HCV infection. All studies had to report either the rate of SAEs for safety and/or successful SVR-12 for efficacy at a minimum. Non-RCTs and studies with the wrong intervention were excluded.

Two databases, PubMed and Cochrane Library, were searched through September 2021 using the following search string: (“Sofosbuvir”[tiab] or GS-7977[MH] or PSI 7977[MH] or PSI-7977[MH] or PSI7977[MH] or Sovaldi[MH]) AND (“Ribavirin”[tiab] or ICN-1229[MH] or Ribetol[MH] or Ribamide[MH] or Ribamidi[MH] or Ribamidy[MH] or RibaspHERE[MH] or Ribovirin[MH] or Tribavirin[MH] or Vilona[MH] or Viramide[MH] or Virazide[MH] or Virazole[MH]) AND (“Hepatitis C”[tiab] or “Hep C”[tiab] or “HCV”[tiab] or PT-NANBH[MH] or Parenterally Transmitted Non-A, Non-B Hepatitis[MH] or Hepatitis, Viral, Non-A, Non-B, Parenterally-Transmitted[MH]) AND (“Random”)). The search was not restricted by languages, year of publication, or publication status using any automation tool. Two investigators independently used the aforementioned string to conduct the search and screened the full results manually to identify all eligible studies.

2.3 | Data extraction

Two primary investigators independently extracted the data from included studies in parallel. Results were compared, and any disagreements were resolved through discussion or seeking input from the senior investigator. The extracted data included National Clinical Trial (NCT) identifier number, the first author’s last name, year of publication, trial location, masking status, trial phase, compared interventions and their duration, HCV GTs, prior treatment experiences (treatment naïve/TN or treatment experienced/TE), cirrhosis status, comorbidities, mean age, total number of randomized participants, and percent males. Additionally, we extracted the number of HCV participants who experienced any SAE and/or successfully achieved SVR-12 in SOF ± RBV intervention for each RCT.

2.4 | Risk of bias

Quality assessment was conducted using the Cochrane Risk of Bias tool, which evaluates randomization, allocation concealment, masking, incomplete or selective reporting, and external sources of bias.\(^16\) Overall RCT quality was defined as low, moderate, or high if more than 3, 2–3, or less than 2 criteria were unmet or insufficiently described, respectively.
Clinical outcomes of interest were pooled and analysed as risk ratios (RR) using a random effects model (DerSimonian-Laird Method) to account for both within study and between study variation. The $I^2$ statistic was used as a measure of heterogeneity, with the following thresholds used for interpretation of heterogeneity: less than 30% (low), 30%–59.99% (moderate), 60%–74.99% (substantial) and 75%–100% (considerable). To investigate heterogeneity, subgroup analysis was performed on pre-specified key characteristics: HCV GTs, the participants’ prior treatment experiences (TN or TE), cirrhosis status, and trial interventions. Influence analysis was further performed to determine the main contributors to heterogeneity, if any. Publication bias was visually evaluated by the funnel plot and confirmed by the statistical Egger’s test. All analyses were conducted using the meta and metafor packages in the R version 4.1.2 with a $P$-value $\leq 0.05$ (95% confidence interval [CI]) set as a statistically significant level.

3 | RESULTS AND DISCUSSION

3.1 | Literature search results

Our search strategy returned 579 records from PubMed and the Cochrane Library, with 202 duplicate records. After initial title and abstract screening, 211 records were sought for article retrieval, and 114 were assessed for eligibility. Out of 114 reports, 88 were excluded because studies were (1) nonrandomized, (2) duplicates of included studies, (3) with ineligible intervention, (4) withdrawn, or (5) still ongoing. For only one eligible RCT (QUANTUM)\(^{17}\) with no data reported on the outcomes in the original record, efficacy and safety results were extracted from another record\(^{18}\) of the same study where trial results were available. A total final of 26 RCTs were included in the current study. The results of the search strategy are presented in the PRISMA flow diagram in Figure 1.\(^{19}\)

3.2 | Study characteristics

Table 1 shows the key characteristics for the 26 trials\(^{17,18,20–42}\) included in this study. All trials were peer-reviewed and published except QUANTUM\(^{17,18}\) and LIVE-C-Free,\(^{28}\) which were originally identified through the Cochrane Library. The location of 16 out of 26 trials was the U.S., where SOF manufacturer located. Other trial locations were Australia, Canada, Egypt, Europe, Japan, and New Zealand. All trials, except QUANTUM\(^{17,18}\) and SIRIUS,\(^{41}\) were open-label, and most were phase 2 randomized trials. The most common compared intervention among the included RCTs was SOF + LDV ± RBV ($n = 12$), followed by SOF + VEL ± RBV intervention ($n = 5$). Duration of the compared interventions ranged from 8 to 24 weeks.

The 26 RCTs included a total of 5058 randomized HCV patients. Most participants were infected with HCV GT1, had no prior HCV treatment experience (i.e., TN), and were noncirrhotic. No trials included participants with GT5 or 6. Both GALAXY\(^{25}\) and LIVE-C-Free\(^{28}\) trials included HCV patients with liver transplant, while ASTRAL-4\(^{21}\) and NCT02996682\(^{39}\) trials included HCV patients with decompensated cirrhosis. The mean age of all participants was 54 years and percent males ranged from 39% to 95%.

3.3 | Risk of bias

Quality assessment results, based on the Cochrane Risk of Bias tool,\(^{16}\) are shown in Figure 2. Out of 26 studies, only the SIRIUS\(^{41}\) trial was of high quality, while the rest were of moderate quality. While industry funding was recognized as an external source of potential bias, the low-quality rating has been mostly attributed to trials being open-label and an insufficient description of allocation concealment.

3.4 | Meta-analysis

The rate of SAEs in patients treated with SOF-based medication regimens with and without RBV was reported by all studies. The pooled RR of SAE was 1.07 (95% CI: 0.77–1.48), indicating that there was no significant difference in SAEs with the addition of RBV to SOF-based medication regimens (Figure 3). Heterogeneity assessment by $I^2$ showed a value of 10% ($p = 0.32$), suggesting that studies were largely homogeneous for this outcome. The symmetry found in the funnel plot through visual inspection indicates no significant evidence of publication bias, as shown in Figure 4, which was confirmed by the Egger regression value of 0.58 ($p = 0.569$).
The number of patients who successfully achieved SVR-12 with SOF-based medication regimens ± RBV was reported by all studies. The pooled RR of SVR-12 was 1.00 (95% CI: 0.98–1.01), indicating that the addition of RBV to SOF-based medication regimens did not significantly increase nor decrease the overall efficacy of the treatment (Figure 5). However, the analysis revealed an I² value of 41% (p < 0.05), suggesting moderate heterogeneity among included studies for this outcome, which was further investigated through subgroup and influence analyses. Symmetry was found in the overall SVR-12 funnel plot, providing no evidence of publication bias (Figure 6), which was confirmed by the Egger regression value of −0.75 (p = 0.460).

### 3.5 | Subgroup analyses

To investigate heterogeneity in SVR-12 outcome, subgroup analyses were performed for HCV GTs, participants’ prior treatment

### TABLE 1

| RCT       | Author (Year) | Country                                                                 | Comparison                                                                 | Participants                                                                 | Age* | ITT | Male (%) |
|-----------|---------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|------|-----|----------|
| A534820   | Tam (2017)    | United States                                                           | SOF + LDV ± RBV                                                           | GT1 TE w/wo Cirrhosis, H1V                                                      | 55   | 7   | 71       |
| ASTRAL-421 | Curry (2015)  | United States                                                           | SOF + VEL ± RBV                                                           | Mix Both Cirrhosis                                                            | 58   | 267| 70       |
| C-ISLE22  | Foster (2018) | United Kingdom                                                          | SOF + EBR/GZR ± RBV                                                       | GT3 Both Cirrhosis                                                            | 54   | 100| 68       |
| COSMOS23  | Lawitz (2014) | United States                                                           | SOF + SMV ± RBV                                                           | GT1 Both w/wo Cirrhosis                                                       | 57   | 167| 64       |
| ELECTRON24 | Gane (2014)   | New Zealand                                                             | SOF + LDV ± RBV                                                           | GT1 TE Cirrhosis                                                              | 59   | 19 | 95       |
| GALAXY25  | O’Leary (2017)| United States                                                           | SOF + SMV ± RBV                                                           | GT1 – Noncirrhotic post liver transplantation                                  | 60   | 33 | 70       |
| ION-126   | Afdhal (2014) | France, Germany, Italy, Spain, the United Kingdom and the United States | SOF + LDV ± RBV                                                           | GT1 TN w/wo Cirrhosis                                                        | 53   | 865| 59       |
| ION-226   | Afdhal (2014) | United States                                                           | SOF + LDV ± RBV                                                           | GT1 TE w/wo Cirrhosis                                                        | 56   | 440| 65       |
| ION-327   | Kowdley (2014)| United States                                                           | SOF + LDV ± RBV                                                           | GT1 TN Noncirrhotic                                                           | 52   | 647| 58       |
| LIVE-C-Free28 | –           | United States                                                           | SOF + LDV ± RBV                                                           | GT1 Both Post liver transplantation                                           | 61   | 32 | 69       |
| LONESTAR29 | Lawitz (2014) | United States                                                           | SOF + LDV ± RBV                                                           | GT1 Both w/wo Cirrhosis                                                       | 50   | 100| 66       |
| NCT01359644 | Sulkowski (2014)| United States                                                          | SOF + DCD ± RBV                                                           | Mix Both Noncirrhotic                                                         | 52   | 211| 53       |
| NCT01826981 | Gane (2015)  | New Zealand                                                             | SOF + LDV ± RBV                                                           | GT3 TN w/wo Cirrhosis                                                        | 46   | 51 | 47       |
| NCT01858766 | Everson (2015)| United States                                                           | SOF + VEL ± RBV                                                           | Mix TN Noncirrhotic                                                           | 53   | 223| 54       |
| NCT01909804 | Pianko (2015) | Australia, New Zealand and the United States                            | SOF + VEL ± RBV                                                           | Mix TE w/wo Cirrhosis                                                        | 55   | 321| 69       |
| NCT01975675 | Mizokami (2015)| Japan                                                                 | SOF + LDV ± RBV                                                           | GT1 Both w/wo Cirrhosis                                                       | 59   | 341| 42       |
| NCT02371408 | Esmat (2017) | Egypt                                                                   | SOF + RSV ± RBV                                                           | GT4 Both w/wo Cirrhosis                                                       | 47   | 228| 65       |
| NCT02487030 | Shiha (2018)  | Egypt                                                                   | SOF + LDV ± RBV                                                           | GT4 Both w/wo Cirrhosis                                                       | 50   | 244| 61       |
| NCT02536313 | Lawitz (2017) | United States                                                           | SOF + VEL + VOX ± RBV                                                      | GT1 TE w/wo Cirrhosis                                                        | 54   | 49 | 65       |
| NCT02781558 | Esteban (2018)| Spain                                                                   | SOF + VEL ± RBV                                                           | GT3 Both Cirrhosis                                                            | 51   | 204| 79       |
| NCT02996682 | Takehara (2019)| Japan                                                                | SOF + VEL ± RBV                                                           | Mix Both Cirrhosis                                                            | 66   | 102| 39       |
| QUANTUM17,18 | –                                           | United States                                                           | SOF + GS-0938 ± RBV                                                        | Mix TN w/wo Cirrhosis                                                        | 51   | 104| 56       |
| QUARTZ III40 | Shafran (2018)| Australia, Canada, New Zealand, France, and the United Kingdom         | SOF + OBV/PTV/r ± RBV                                                      | GT3 Both Noncirrhotic                                                         | 53   | 20 | 60       |
| RESCUE20   | Tam (2017)    | Canada and the United States                                             | SOF + LDV ± RBV                                                           | Mix TE w/wo Cirrhosis                                                        | 58   | 82 | 74       |
| SIRIUS41   | Bourlière (2015)| France                                                              | SOF + LDV ± RBV                                                           | GT1 TE Cirrhosis                                                              | 57   | 155| 74       |
| TRILOGY22  | Lawitz (2016) | United States                                                           | SOF + LDV + VDV ± RBV                                                      | GT1 TE Cirrhosis                                                              | 57   | 46 | 65       |

Abbreviations: EBR/GZR, Elbasvir/Grazoprevir; SMV, Simeprevir; DCD, Daclatasvir; RSV, Ravidasvir; OBV/PTV/r, Ombitasvir/Paritaprevir/Ritonavir; VDV, Vedoprevir; Co., Comorbidities; w/wo Cirrhosis, with and without cirrhosis; ITT, Total number of randomized participants (intention to treat).

*Mean age.

Median age.
experiences (TN or TE), cirrhosis status, and trial interventions as shown in Figure 7. All subgroups demonstrated no additional efficacy gain with RBV, except the SOF + VEL subgroup that indicated a slight improvement in efficacy with RBV addition (RR = 0.94, 95% CI: 0.91–0.98); however, the summary RR estimate for this subgroup is still very close to the null effect.

The GT subgroup analysis showed moderate homogeneity among trials involving HCV GT1 participants ($I^2$: 32%, $p = 0.09$), and significantly substantial heterogeneity among trials with HCV GT3 participants ($I^2$: 74%, $p < 0.01$). The analysis results for trials with TE participants are largely homogenous ($I^2$: 12%, $p = 0.32$), while insignificant and moderate heterogeneity still exists among
trials with TN participants ($I^2$: 40%, $p = 0.08$), and trials with both TN and TE participants ($I^2$: 46%, $p = 0.10$). Similarly, trials with non-cirrhotic participants were mainly homogeneous ($I^2$: 28%, $p = 0.19$); however, trials involving only cirrhotic participants had significant but moderate heterogeneity ($I^2$: 51%, $p = 0.03$). Finally, the analysis by trial interventions revealed significant but moderate homogeneity for SOF + LDV ± RBV intervention ($I^2$: 45%, $p = 0.04$) and insignificantly low heterogeneity for the SOF + VEL ± RBV intervention ($I^2$: 3%, $p = 0.39$). Throughout the subgroup analyses, NCT01826981$^{31}$ and ASTRAL-4$^{21}$ consistently contributed to the observed heterogeneity.

### 3.6 Influence analysis

Results of the influence analysis (Figure 8) of SVR-12 showed that NCT01826981$^{31}$ was the main source of heterogeneity in this

![Funnel plot of risk ratio for SVR-12](image)

**Figure 6** Funnel plot of risk ratio for SVR-12

![Forest plot of risk ratio of achieving SVR-12](image)

**Figure 7** Forest plot of risk ratio of achieving SVR-12 by (A) prior treatment status (B) cirrhosis status (C) genotype (D) study intervention
outcome. This study alone contributed approximately one-third of the heterogeneity in the overall SVR-12 analysis. After omitting this trial, the RR summary estimate still showed no difference in SVR-12 with and without RBV (RR = 1.00, 95% CI: 0.99–1.01), while the $I^2$ dropped from 41.3% (moderate heterogeneity) to 28.7% (low heterogeneity).
4 | DISCUSSION

Our systematic review and meta-analyses involved 26 trials with 5058 HCV patients. Based on the currently available evidence, our analyses revealed that adding RBV to SOF-based medication regimens neither posed serious harms (SAEs RR = 1.07, 95% CI: 0.77–1.48) nor provided a clinical benefit (SVR-12 RR = 1.00, 95% CI: 0.98–1.01).

Lack of benefit persisted among HCV patients regardless of their HCV GT, prior treatment experience, cirrhosis status, and trial intervention. Overall, trials showed moderate homogeneity regarding efficacy except among participants with HCV GT3, a GT that has the worst prognosis and is difficult to treat.\(^{43}\) However, the measure of heterogeneity in this subgroup may be overestimated, given the small number of HCV GT3 studies (\(n = 5\)).\(^{44}\) Additionally, the individual CI of four GT3 trials\(^{22,33,38,40}\) visually overlapped, while NCT01826981\(^{31}\) uniquely did not. In fact, this NCT01826981\(^{31}\) trial has consistently been an outlier without an obvious explanation based on its characteristics. NCT01826981\(^{31}\) was an open-label trial from New Zealand that included TN patients with GT3 only, compared SOF + LDV ± RBV for 12 weeks each, and showed significantly higher efficacy with RBV addition. The exclusion of this trial reduced heterogeneity but did not impact our initial finding: no difference in overall efficacy of SOF-based medication regimens with and without RBV.

Our results were consistent with other previously published meta-analyses evaluating safety and efficacy of SOF-based medication regimens with and without RBV in HCV GT1 patients.\(^{45-50}\) Meta-analysis studies comparing SOF + LDV ± RBV in this GT revealed that adding RBV did not pose serious harms\(^{45,46}\) nor was this associated with any efficacy improvement.\(^{45-48}\) Another meta-analysis comparing efficacy of the same intervention in HCV GT1 but limited to cirrhotic patients with prior treatment experience also showed SOF + LDV to be as efficacious as SOF + LDV + RBV.\(^{49}\) A meta-analysis examining another intervention (SOF + VEL ± RBV) consistently revealed a lack of efficacy improvement with RBV addition in HCV GT1 patients.\(^{50}\)

While the results of HCV GT1 meta-analyses were consistent in the literature and matched our findings of no clinical benefit of adding RBV to SOF-based medication regimens, HCV GT3 meta-analyses had inconclusive results.\(^{51,52}\) A meta-analysis by Ampuero et al., testing the impact of RBV on multiple SOF-based medication regimens (SOF + DCV and SOF + LDV) among GT3 HCV patients, revealed that the addition of RBV showed no difference on the efficacy of SOF + DCV, and a higher efficacy for SOF + LDV.\(^{51}\) However, results from the Ampuero et al. meta-analysis\(^ {51}\) are limited by inappropriately using the fixed effect model\(^ {53}\) for studies with different designs (randomized and non-randomized trials) and including a small number of studies (\(n = 2\)) in the SOF + LDV + RBV analysis, one of which (NCT01826981\(^ {31}\)) was identified as an outlier in our analysis. In contrast, our meta-analysis addresses these limitations by including a greater number of trials in the HCV GT3 subgroup (\(n = 5\)) with a consistent RCT design. Another recent network meta-analysis\(^ {52}\) recommended RBV addition in HCV GT3 patients; however, their indirect comparisons within three unconnected networks lacked coherence assessment which may affect the validity of their results.

The current literature does not have many studies involving SOF-based medication regimens in HCV patients with complications who are known to have a poor prognosis. In our study, post-liver transplantation HCV patients in GALAXY\(^ {25}\) and LIVE-C-Free\(^ {28}\) trials insignificantly favoured two different SOF-based medication regimens without RBV. Both were U.S.-based open-label trials with GT1 patients and compared SOF + SMV ± RBV (GALAXY\(^ {25}\)) and SOF + LDV ± RBV (LIVE-C-Free\(^ {28}\)). Our study also included patients with
decompensated cirrhosis in NCT02996682 and ASTRAL-4 trials. The NCT02996682 trial showed no additional efficacy gain with RBV, similar to our overall efficacy result. This trial was an open-label Japanese RCT comparing SOF + VEL + RBV in both TN and TE HCV patients with mainly GT1 (78%). Despite having the same characteristics as the NCT02996682 trial, except for study location, the U.S.-based ASTRAL-4 trial significantly favoured RBV addition. Based on our analysis, ASTRAL-4 was the second highest contributor to the efficacy heterogeneity with no specific explanation.

Our study is the first to comprehensively investigate the impact of RBV addition to any SOF-based medication regimen. The large number of included trials and the narrow CI of the observed RR illustrate the precision and reliability of our analyses and findings. Overall participants had diverse HCV GTs, prior treatment experiences, cirrhosis status, and complications such as liver transplantation and decompensated cirrhosis. However, this study is limited by trials with a moderate risk of bias. In addition, no trials had patients with HCV GT 5 or 6; therefore, our findings could only be extrapolated across HCV GT 1 through 4. A future update of our meta-analysis would ideally include trials with HCV GT 5 and 6 patients.

5  WHAT IS NEW AND CONCLUSION

In conclusion, the addition of RBV to SOF-based medication regimens did not increase harm nor did it provide clinical benefits in HCV patients based on the current evidence with moderate risk of bias. These findings do not support using RBV with SOF-based medication regimens among HCV patients with different clinical scenarios. Further investigations would be needed to confirm our results and reflect on clinical practice.

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CONFLICT OF INTEREST

All authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the authors upon reasonable request.

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