ISSN 1948-5182 (online)

World Journal of *Hepatology*

World J Hepatol 2023 February 27; 15(2): 123-320

Published by Baishideng Publishing Group Inc

World Journal of Hepatology

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The *WJH* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for *WJH* as 0.52. The *WJH*'s CiteScore for 2021 is 3.6 and Scopus CiteScore rank 2021: Hepatology is 42/70.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yi-Xuan Cai*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Xiang Li*.

NAME OF JOURNAL
World Journal of Hepatology

ISSN
ISSN 1948-5182 (online)

LAUNCH DATE
October 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Nikolaos Pyrsopoulos, Ke-Qin Hu, Koo Jeong Kang

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https://www.wjgnet.com/1948-5182/editorialboard.htm

PUBLICATION DATE
February 27, 2023

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World Journal of Hepatology

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World J Hepatol 2023 February 27; 15(2): 318-320

DOI: 10.4254/wjh.v15.i2.318

ISSN 1948-5182 (online)

LETTER TO THE EDITOR

Glecaprevir/pibrentasvir + sofosbuvir for post-liver transplant recurrent hepatitis C virus treatment

Rishi Arora, Michelle T Martin, Justin Boike, Sonalie Patel

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Heo J, South Korea; Vij M, India; Yang SS, Taiwan

Received: December 9, 2022
Peer-review started: December 9, 2022
First decision: December 24, 2022
Revised: December 30, 2022
Accepted: January 17, 2023
Article in press: January 17, 2023
Published online: February 27, 2023

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Abstract

Glecaprevir/pibrentasvir in combination with sofosbuvir may serve as a safe and effective option for treatment of recurrent hepatitis C virus post-liver transplant in patients who previously failed direct-acting antivirals.

Key Words: Hepatitis C virus; Direct-acting antivirals; Liver transplantation; Glecaprevir/pibrentasvir; Sofosbuvir; Ribavirin

Core Tip: In the post-liver transplant population, current national guidance only recommends sofosbuvir/velpatasvir/voxilaprevir, with or without ribavirin, for recurrent hepatitis C virus treatment in direct-acting antiviral-experienced patients. We describe an alternative regimen of glecaprevir/pibrentasvir in combination with sofosbuvir that resulted in sustained virologic response without treatment-related adverse events.

Citation: Arora R, Martin MT, Boike J, Patel S. Glecaprevir/pibrentasvir + sofosbuvir for post-liver transplant recurrent hepatitis C virus treatment. *World J Hepatol* 2023; 15(2): 318-320
URL: https://www.wjgnet.com/1948-5182/full/v15/i2/318.htm
DOI: https://dx.doi.org/10.4254/wjh.v15.i2.318

TO THE EDITOR

For direct-acting antiviral-experienced patients with recurrent hepatitis C virus (HCV), current national guidance recommends treatment with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) or glecaprevir/pibrentasvir (GLE/PIB) and sofosbuvir in combination with ribavirin (RBV) due to their established safety and efficacy profiles. However, for recurrent HCV treatment post-liver transplant, guidance recommends use of SOF/VEL/VOX +/- RBV for 12 wk. This recommendation is based on expert consensus from seven total cases, none of which included patients who failed SOF/VEL/VOX pre-transplant[1-3]. Current guidance does not provide any recommendation for the use of GLE/PIB with SOF +/- RBV post-liver transplant, and we are unaware of published studies describing its use in direct-acting antiviral-experienced patients with recurrent HCV post-liver transplant.

We report outcomes of recurrent HCV in two patients with a history of compensated cirrhosis and hepatocellular carcinoma treated with Y90 radioembolization who underwent 24 wk of GLE/PIB with SOF after orthotopic liver transplantation from HCV-negative donors. RBV was not started in either patient due to hemoglobin < 100 g/L at treatment initiation. At the time of transplant, Model for End-Stage Liver Disease – Sodium scores were 11 and 9 for patient 1 and 2, respectively. Neither patient was co-infected with HIV or hepatitis B virus. Patient 1, a 71-year-old man with genotype 3 HCV, failed two treatments pre-transplant: (1) 12 wk of SOF/VEL; and (2) 12 wk of SOF/VEL/VOX after the patient developed hepatocellular carcinoma. Subsequent resistance testing found no mutations. Patient 2, a 67-year-old man with genotype 1 HCV, failed four regimens pre-transplant: (1) Pegylated interferon + RBV + SOF; (2) 24 wk of ledipasvir/sofosbuvir; (3) 12 wk of GLE/PIB; and (4) 12 wk of SOF/VEL/VOX and RBV. Treatment courses three and four occurred after the patient developed hepatocellular carcinoma. Subsequent resistance testing detected Q30R and Y93N mutations.

Prior to treatment initiation but post-transplantation, HCV RNA resulted as 337 and 667114 IU/mL for patient 1 and 2, respectively. After 4 wk of treatment, HCV RNA levels were undetected and remained undetected throughout treatment. Both patients achieved sustained virologic response at 12 wk after treatment completion. Minor tacrolimus dose reductions were made in the immediate post-transplantation period, but neither patient achieved toxic levels. Neither patient experienced any treatment-related adverse events, transplant complications, acute cellular rejection, or antibody-mediated rejection during and through 12 wk post-treatment completion.

Drug-drug interactions between direct-acting antivirals and immunosuppressants must be carefully considered before use. A 1.5-fold increase in tacrolimus area under the curve can occur with GLE/PIB co-administration; therefore, therapeutic drug monitoring is imperative and tacrolimus dose reductions may be needed during treatment. In those individuals taking cyclosporine, doses should be limited to < 0.1 g/d because higher doses can increase glecaprevir exposure, which may lead to increased risk of adverse events. HCV in the post-transplant setting can cause rapid development of fibrosis and decompensation, leading to higher rates of rejection, graft failure, and mortality[4]. Direct-acting antivirals offer high cure rates, but in patients who fail to achieve sustained virologic response prior to liver transplant, national guidance offers limited recommendations for recurrent HCV treatment post-transplant. Use of GLE/PIB with SOF for 24 wk offered an effective alternative to SOF/VEL/VOX +/- RBV in this small, yet complex cohort of patients and may be considered in patients who failed SOF/VEL/VOX pre-liver transplant.

FOOTNOTES

Author contributions: Arora R and Patel S led and Martin MT and Boike J assisted with the study concept and design; Arora R and Patel S equally contributed to acquisition of data and analysis and interpretation of data; Arora R led initial drafting of the manuscript, Patel S led final drafting of the manuscript, and Martin MT and Boike J edited the manuscript; All authors reviewed the manuscript for important intellectual content, gave final approval of data, and are accountable for the work.

Conflict-of-interest statement: Martin MT and Patel S serve on the speakers' bureau for AbbVie and Gilead. Martin MT has received grant funding from Gilead and Merck, served on the advisory board for AbbVie and Gilead, and is a minor shareholder of AbbVie, Gilead, and Merck stock.

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S-Editor: Liu JH
L-Editor: A
P-Editor: Liu JH

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