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Long-term Follow-up of Hepatitis C Patients Who Achieved Sustained Virologic Response in the Pragmatic PRIORITIZE Study

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Multiple real-world studies have confirmed the safety and efficacy of hepatitis C (HCV) direct-acting antivirals (DAAs); however, few studies have provided data on long-term outcomes of patients without cirrhosis after achieving sustained virologic response (SVR).[1–3] The aims of this analysis were to describe, among individuals in the PRIORITIZE Study achieving SVR: (1) the frequency of laboratory testing and imaging during long-term follow-up (LTFU), (2) changes in liver tests, (3) occurrence of hepatic decompensation or hepatocellular carcinoma (HCC) and deaths, and (4) durability of SVR.

The PRIORITZE Study was a randomized, pragmatic clinical trial to compare the effectiveness of 3 DAA regimens for treatment of HCV genotype 1 infection.[1] Patients were

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of Clinical Gastroenterology and Hepatology at www.cghjournal.org, and at http://doi.org/10.1016/j.cgh.2022.01.059.

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managed per standard-of-care at individual sites with no protocol-required study visits or tests. We analyzed the frequency of testing and outcomes of patients who achieved SVR and reached the LTFU period, defined as ≥24 weeks after the end-of-treatment (Supplementary Materials).

A total of 1275 patients started treatment; 1259 reached the LTFU period, of whom 840 had medical records available for review and 771 of 840 patients (91.8%) achieved SVR (Supplementary Table 1). The median age was 59 years, 58.8% were men, 47.2% were Black, and 19.1% had cirrhosis (all compensated). A higher percentage of patients with LTFU data had cirrhosis (19.1% vs 11.5%), were Black (47.2% vs 34.2%), or were older than 39 years (89.6% vs 82.2%) than those without LTFU data.

The percentages of patients with follow-up liver tests during the periods 24 to 48, 48 to 96, and >96 weeks after end-of-treatment were 68%, 73.5%, and 34.7%, respectively, among patients with cirrhosis, and 54.3%, 61.5%, and 23.7%, respectively, for those without cirrhosis. The corresponding percentages for imaging were 44.2%, 54.4%, and 23.8%; and 12.8%, 21%, and 0.2%, respectively, for patients with and those without cirrhosis. Among 240 patients with ≥2 years of LTFU, 61 had cirrhosis, and the median number of ultrasounds performed was 1 per year. Improvement in liver tests was observed in patients with as well as those without cirrhosis, with greater improvement in patients with cirrhosis and during treatment and the first 24 to 48 weeks after the end-of-treatment and plateauing thereafter (Supplementary Figure 1). SVR was durable in all 477 patients (97 with cirrhosis) with follow-up tests.

During a median follow-up of 86.9 weeks (inter-quartile range, 60.1–100.0 weeks) from the end-of-treatment, 10 patients experienced adverse liver outcomes, all had cirrhosis (Figure 1). Three patients had incident HCC, and 2 had metastatic or recurrent HCC. Five patients experienced hepatic decompensation. Nine patients (1.2%) died, 5 patients (3.4%) of 147 patients with and 4 patients (0.6%) of 624 without baseline cirrhosis; 2 were liver-related.

We found that during the LTFU of patients who achieved SVR in the PRIORITIZE Study, laboratory tests and imaging were inconsistently performed. Among the patients who started treatment and had not died or withdrawn, 33% of patients overall and 25.5% of patients with cirrhosis had no follow-up records ≥24 weeks after end-of-treatment, and one-third did not have an HCV RNA test to assess SVR. This troubling trend has also been reported in other real-world studies.[4]

Excluding 2 patients with HCC prior to DAA treatment, only 8 patients (1.0%) had adverse liver outcomes. It has been suggested that DAA therapy leads to earlier HCC recurrence and a higher incidence of HCC compared with interferon-based regimens.[5,6] These findings have not been substantiated.[5,7–10] In this study, 2 patients with a history of HCC were diagnosed to have metastatic or recurrent HCC, and only 3 patients (0.4%) of 769 (1.1% among those with cirrhosis) with no history of HCC were diagnosed with HCC. Five patients (0.6%) experienced hepatic decompensation.

This study included a large real-world cohort managed in multiple centers across the United States. Limitations include a high percentage of patients without LTFU data, although some

patients might have follow-up testing through their primary care physicians, nonstandardized follow-up, and assessment of liver disease regression based on laboratory test results.

We found that LTFU of patients with HCV, who achieved SVR with DAAs, was variable. Sustained improvement in liver tests was observed in patients with as well as those without cirrhosis. Adverse liver outcomes were uncommon and occurred only in patients with cirrhosis, supporting the need for continued follow-up of patients with cirrhosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of interest

These authors disclose the following: Anna S. Lok reports grant funding from Bristol-Myers Squibb; and serves on the advisory board for Gilead, and HCV-TARGET. Kenneth E Sherman reports grants/contracts (paid to institution) by AbbVie, Gilead, Intercept, and Zydus; serves on the advisory board and performs consulting for Gilead and Theratechnologies; and is on the DSMB/adjudication committees for Inovio, MedPace, and Horizon. Mandana Khalili reports grant funding from Gilead Sciences Inc and Intercept Pharmaceuticals; and is a consultant for Gilead Sciences Inc. Dawn Fishbein reports grants from Gilead Focus partnership (past) and Gilead Sciences Inc; owns stock in AbbVie and Merck over the years <$10,000 has been held in discretionary account without any personal authority to buy or sell any stock position; however, her father and brother are the portfolio managers; and served on the Gilead Advisory Board for 2020. K. Rajender Reddy reports grants from Gilead, Intercept, Exact Sciences, HCC-TARGET, HCV-TARGET, NASH-TARGET, Mallinckrodt, Bristol-Myers Squibb, Sequana, and Grifols; reports personal fees from Spark Therapeutics, Novo Nordisk, and Mallinckrodt; and is on the DSMB for Novartis. Brian Pearlman reports grants from AbbVie, Merck, and Gilead; is a consultant for AbbVie, Merck, and Gilead; has done sponsored lectures and received honoraria for AbbVie, Merck, and Gilead. Michael W. Fried reports grants from AbbVie, Bristol-Myers Squibb, Merck, and Gilead; reports personal fees from AbbVie, Bristol-Myers Squibb, Merck, and Roche; reports personal fees and other from TARGET PharmaSolutions, outside the submitted work; reports research grants from the National Institutes of Health; and is a stockholder of TARGET PharmaSolutions. Joy Peter reports that her domestic partner is an AbbVie Stockholder. Jodi B. Segal reports grant funding from the National Institutes of Health, National Institute of Health Care Management, Arnold Foundation, and the United States Food and Drug Administration; is an employee at Johns Hopkins University; and is a contractor for the American College of Physicians. Mark S. Sulkowski reports funds paid to Johns Hopkins University by AbbVie, Assembly Biosciences, Janssen; and is a consultant for AbbVie, Gilead, Antios, GSK, and Assembly Biosciences. David R. Nelson reports grants from AbbVie, Gilead and Merck during the conduct of the study; and is a stockholder of TARGET PharmaSolutions.

Abbreviations used in this paper:

DAA	direct-acting antiviral
HCV	hepatitis C virus
HCC	hepatocellular carcinoma
LTFU	long-term follow-up
SVR	sustained virologic response

References

1. Sulkowski MS, et al. Hepatology 2021;74:2952–2964. [PubMed: 34255381]
2. Backus LI, et al. Antivir Ther 2017;22:481–493. [PubMed: 27934775]
3. Mangia A, et al. Liver Int 2020;40:1841–1852. [PubMed: 32449966]
4. Serper M, et al. J Gen Intern Med 2020;35:1011–1020. [PubMed: 31659661]
5. Conti F, et al. J Hepatol 2016;65:727–733. [PubMed: 27349488]
6. Reig M, et al. J Hepatol 2016;65:719–726. [PubMed: 27084592]
7. ANRS Collaborative Study Group on Hepatocellular Carcinoma. J Hepatol 2017;65:734–740.
8. Singal AG, et al. Gastroenterology 2019;156:1683–1692.e1. [PubMed: 30660729]
9. Kanwal F, et al. Gastroenterology 2017;153:996–1005.e1. [PubMed: 28642197]
10. Ioannou GN, et al. J Hepatol 2018;68:25–32.

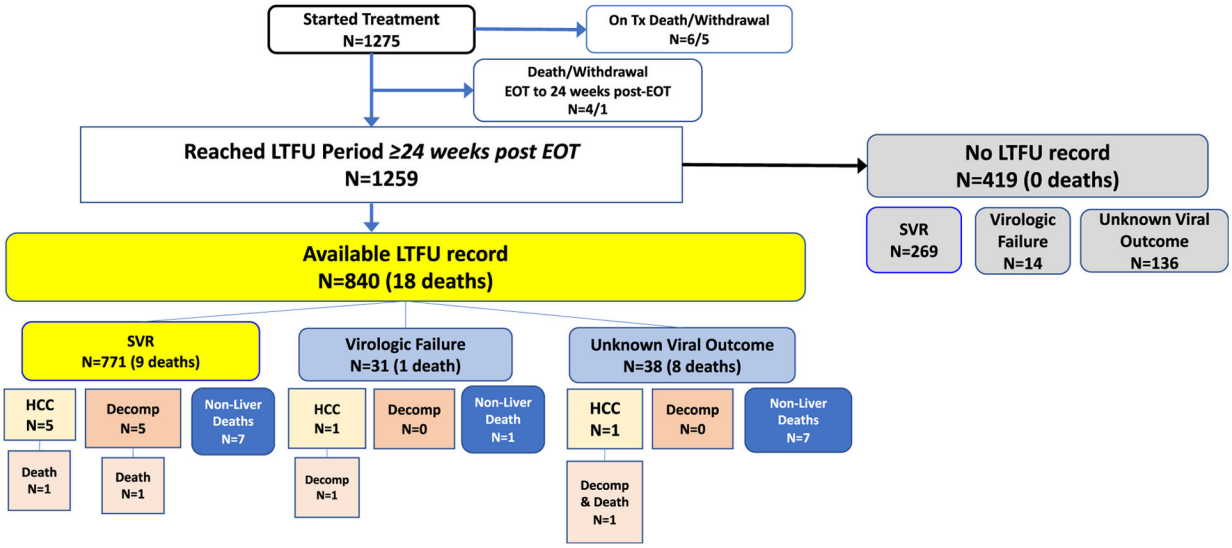

Figure 1.

Flow chart showing outcomes of 1275 patients who started treatment; 1259 reached the LTFU period. Of these, 840 had LTFU data of whom 771 achieved SVR. *Decomp*, Hepatic decompensation; *EOT*, end-of-treatment.