DO YOU SEE CHRONIC HCV PATIENTS WITH CHALLENGES LIKE BRIAN'S?

Brian, 28

GENOTYPE 3

NON-CIRRHOTIC: F2

FOOD INSECURITIES

INJECTION DRUG USE

Not an actual patient.

Treat confidently with EPCLUSA:
an answer for your real patient challenges[1,2]

INDICATION

EPCLUSA (sofosbuvir 400 mg/velpatasvir 100 mg, sofosbuvir 200 mg/velpatasvir 50 mg tablets) is indicated for the treatment of patients 6 years of age and older or weighing at least 17 kg with chronic hepatitis C virus (HCV) genotype 1-6 infection without cirrhosis or with compensated cirrhosis and in combination with ribavirin for those with decompensated cirrhosis.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV: Hepatitis B virus (HBV) reactivation has been reported, in some cases resulting in fulminant hepatitis, hepatic failure, and death.

Click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

F2 = stage 2 fibrosis.

EPCLUSA®
sofosbuvir/velpatasvir
400 mg/100 mg tablets

CHALLENGING TIMES DEMAND **REAL ACTION**

New HCV infections are on the rise due to the opioid epidemic and injection drug use[3]

44K

ESTIMATED **NEW** ACUTE HCV CASES IN 2017[4]

Acute cases **INCREASED** over the past decade (2010-2017) due to increased injection drug use[5]

The **most rapid increase** in incidence has been in **adults aged 20-39 years** who inject drugs[5]

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN HCV/HBV COINFECTED PATIENTS

Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with EPCLUSA. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct-acting antivirals (DAAs) and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Cases have been reported in patients who are HBsAg positive, in patients with serologic evidence of resolved HBV, and also in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV DAAs may be increased in patients taking these other agents. Monitor HCV/HBV coinfected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.

AASLD = American Association for the Study of Liver Diseases; CDC = Centers for Disease Control and Prevention; IDSA = Infectious Diseases Society of America; USPSTF = United States Preventive Services Task Force.

GUIDELINES RECOMMEND **BROAD HCV SCREENING** AND THE NEED FOR LINKAGE TO CARE AND TREATMENT[5-7]

AASLD/IDSA, CDC[a]**,** and **USPSTF**[b] all independently recommend a one-time universal HCV screening for all adults

AASLD/IDSA, CDC, and **USPSTF** also independently recommend HCV screening for at-risk patients

> **THE MOST IMPORTANT RISK FACTOR FOR HCV INFECTION IS PAST OR CURRENT INJECTION DRUG USE”**
>
> —USPSTF 2020 Recommendation Statement[5]

> **“ACTIVE OR RECENT DRUG USE OR A CONCERN FOR REINFECTION IS NOT A CONTRAINDICATION TO HCV TREATMENT**
>
> —AASLD/IDSA 2018 Recommendations for Testing, Managing, and Treating Hepatitis C[6]

Reduce the risk of HCV in the community by **screening and treating high-risk patients**[5,6]

[a]Except in settings where the prevalence of HCV infection (HCV RNA-positivity) is <0.1 %.[7]
[b]Recommendations for screening of adults (18-79).[5]

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HAVE CONFIDENCE IN CONSISTENT OUTCOMES FOR CHALLENGING POPULATIONS

ASTRAL PIVOTAL TRIALS

98% **overall cure rate in clinical trials in GT 1-6 NC/CC adult patients**
(n=1015/1035; ASTRAL-1, -2, -3 studies).[1]

SVR12 was the primary endpoint in EPCLUSA clinical trials and was defined as HCV RNA <15 IU/mL at 12 weeks after the end of treatment.[2,3] Achieving SVR is considered a virologic cure.[1,8-10]

EPCLUSA demonstrated high cure rates in people who inject drugs in SIMPLIFY & ANCHOR

SIMPLIFY CLINICAL STUDY

94% **cure rate in a clinical study in GT 1-4 NC/CC adult patients**
(n=97/103)[9]

ANCHOR REAL-WORLD STUDY

88% **cure rate in a real-world study in GT 1-4 NC/CC adult patients**
(n=82/93; PP)[10]

For the total population, the SVR12 rate was 82% (n=82/100).[10]

Both studies had a primary endpoint of SVR12 (HCV RNA <LLOQ 12 weeks after treatment completion).[1,8-10]

TRIAL SAFETY DATA (ASTRAL)

- Adverse reactions (all grades) reported in ≥5% of all adult patients receiving 12 weeks of treatment with EPCLUSA (ASTRAL-1, -2, -3): headache, fatigue, nausea, asthenia, and insomnia. Irritability was also observed in ≥5% of adult patients receiving EPCLUSA in ASTRAL-3.[1]

TRIAL SAFETY DATA (SIMPLIFY)

- Adverse reactions reported in ≥5% of adult patients were: fatigue (22%), headache (18%), nausea (14%), insomnia (9%), arthralgia (6%), dizziness (5%), and nasopharyngitis (5%).[9]
- Seven (7%) adult patients had at least one serious adverse event and 1 (1%) was considered treatment-related.[9]

Please see Study Designs on the right for complete details.

EPCLUSA provided a consistent cure in people who inject drugs with varied adherence[9]

Patients in SIMPLIFY and ANCHOR were instructed to use EPCLUSA once daily for 12 weeks as recommended in the EPCLUSA full Prescribing Information. In SIMPLIFY, patients received EPCLUSA in weekly blister packs.

Real-world data are observational in nature and are not based on controlled clinical studies. **Results from these studies may differ from those observed in clinical practice and are not presented in the EPCLUSA Prescribing Information.[1,9,10]**

The SIMPLIFY and ANCHOR studies were supported by Gilead Sciences, Inc.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- If EPCLUSA is used in combination with ribavirin (RBV), all contraindications, warnings and precautions, in particular pregnancy avoidance, and adverse reactions to RBV also apply. Refer to RBV prescribing information.

CC = compensated cirrhosis; GT = genotype; LLOQ = lower limit of quantification; NC = non-cirrhotic; OAT = opioid agonist therapy; Peg-IFN = peginterferon alfa; PP = per protocol; RBV = ribavirin; SOF = sofosbuvir; SVR = sustained virologic response. TE = treatment-experienced; TN = treatment-naïve; VL = viral load.

STUDY DESIGNS

ASTRAL

Randomized trials in TN and TE adult chronic HCV patients without cirrhosis or with compensated cirrhosis.[1]

Patients who were active injection drug users (use within 12 months), or those with a positive urine drug test at screening, were excluded from the ASTRAL pivotal trials.[11,12]

ASTRAL-1: Double-blind, placebo-controlled trial in GT 1, 2, 4, 5, or 6 patients (N=740). GT 1, 2, 4, or 6 patients were randomized 5:1 to receive EPCLUSA or placebo for 12 weeks; GT 5 subjects received EPCLUSA for 12 weeks.[1]

ASTRAL-2: Open-label trial in GT 2 subjects (N=266). Patients received EPCLUSA or SOF + RBV for 12 weeks.[1]

ASTRAL-3: Open-label trial in GT 3 subjects (N=552). Patients received EPCLUSA for 12 weeks or SOF + RBV for 24 weeks.[1]

TE patients had failed a Peg-IFN + RBV-based regimen with or without an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir).[1]

SIMPLIFY

SIMPLIFY was an open-label, single-arm, international Phase 4 trial aimed at evaluating the efficacy, safety, and adherence of EPCLUSA for 12 weeks in GT 1-6 adults with recent injection drug use (within 6 months) and naïve to NS5A-based HCV therapy (N=103). Patients with HIV and/or decompensated liver disease were excluded. The primary endpoint was the proportion of participants with SVR12. Adherence (≥90%) was a secondary endpoint and was assessed by dividing the number of total doses received by total expected number of doses.[9]

Study Limitations: Weekly clinic visits and weekly electronic blister packs, which patients were incentivized to return, may have led to improved adherence, which may not be generalizable to the larger HCV population. The study population in SIMPLIFY was recruited from hospital-based and community-based clinics/centers; it may not be generalizable to all populations of people with injection drug use.[9]

ANCHOR

ANCHOR was a prospective, open-label, observational, single-site trial evaluating the efficacy and adherence of EPCLUSA for 12 weeks in adults with opioid use disorder and reported ongoing injection drug use (within 3 months of screening visit) treated at a harm-reduction center in Washington, DC (N=100). Participants were offered optional buprenorphine initiation. Patients with decompensated liver disease and those who were pregnant or breastfeeding were excluded. The primary endpoint was the proportion of participants with SVR12. Adherence was assessed by monthly pill count, HCV VL, number of bottles completed, interruptions on treatment (≥3 days with resumption), and date of last pill taken relative to planned end of treatment date. Imperfect daily adherence was defined as finishing treatment >7 days after the anticipated treatment end date.[10]

Study Limitations: OAT status groups were non-randomized and self-selected. Factors associated with non-uptake or discontinuation of OAT may have been the same factors that led to HCV treatment failure or loss to follow-up. Results may not be generalizable to the larger HCV population.[10]

The SIMPLIFY and ANCHOR studies are not presented in the EPCLUSA full Prescribing Information.

Click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

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A REAL COMMITMENT TO **CURE**

Safety and efficacy demonstrated in unique prospective studies **focused solely on people who inject drugs**[9,10]

SIMPLIFY CLINICAL STUDY	**ANCHOR** REAL-WORLD STUDY
A prospective clinical trial that assessed efficacy and safety of EPCLUSA in **people who inject drugs**[9]	A study that evaluated the efficacy of EPCLUSA in HCV **patients who inject drugs** and their real challenges in a **real-world setting**[10]

MAIN TAKEAWAYS[10]

- All participants self-reported injection drug use within 3-6 months of enrollment
- Many participants were concurrently on medication-assisted treatment
- Impact of adherence on efficacy with EPCLUSA was assessed

Patients in SIMPLIFY and ANCHOR were instructed to use EPCLUSA for 12 weeks as recommended in the EPCLUSA full Prescribing Information.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Serious Symptomatic Bradycardia When Coadministered with Amiodarone:** Amiodarone is not recommended for use with EPCLUSA due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. A fatal cardiac arrest was reported in a patient taking amiodarone who was coadministered a sofosbuvir-containing regimen. In patients without alternative viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.
- **Risk of Reduced Therapeutic Effect Due to Concomitant Use of EPCLUSA with P-gp Inducers and/or Moderate to Strong Inducers of CYP2B6, CYP2C8 or CYP3A4:** Rifampin, St. John's wort, and carbamazepine are not recommended for use with EPCLUSA as they may significantly decrease sofosbuvir and/or velpatasvir plasma concentrations.

ADVERSE REACTIONS

- The most common adverse reactions (≥10%, all grades) with EPCLUSA were headache and fatigue; and when used with RBV in decompensated cirrhotics were fatigue, anemia, nausea, headache, insomnia, and diarrhea.

CC = compensated cirrhosis; NC = non-cirrhotic.

REAL ATTRIBUTES FOR THE REAL CHALLENGES ASSOCIATED WITH **INJECTION DRUG USE**

NO KNOWN INTERACTIONS WITH:
- Opioids oxycodone and fentanyl
- Antipsychotics aripiprazole (ABILIFY), clozapine (CLOZARIL), and quetiapine (SEROQUEL)[13]

NO FOOD REQUIREMENT
in NC/CC patients, so patients can take with or without food[1]

Effective with **CONCURRENT MAT**[9]

PROTEASE INHIBITOR–FREE[1]

MINIMAL PILL BURDEN[1]
One pill, once a day for 12 weeks in NC/CC patients

In patients with decompensated cirrhosis, EPCLUSA is used with ribavirin, which is dosed by weight

AVAILABLE IN MONTHLY BOTTLES,
which may enable patients with unstable housing to be discreet

EPCLUSA provided a consistent cure in people who inject drugs with varied adherence

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Cure = sustained virologic response (SVR12; HCV RNA <LLOQ 12 weeks after treatment completion)[8]

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SOFOSBUVIR /VELPATASVIR:

THE ONLY PROTEASE INHIBITOR–FREE, PANGENOTYPIC, PANFIBROTIC HCV REGIMEN FOR A BROAD RANGE OF PATIENTS[1,2]

Not actual patients.

Safety and efficacy demonstrated in unique prospective studies focused solely on **people who inject drugs**[9,10]

The SIMPLIFY and ANCHOR studies are not presented in the EPCLUSA full Prescribing Information.

IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS

- Coadministration of EPCLUSA is not recommended with topotecan due to increased concentrations of topotecan.
- Coadministration of EPCLUSA is not recommended with proton-pump inhibitors, phenobarbital, phenytoin, rifabutin, rifapentine, efavirenz, and tipranavir/ritonavir due to decreased concentrations of sofosbuvir and/or velpatasvir.

Consult the full Prescribing Information for EPCLUSA for more information on potentially significant drug interactions, including clinical comments.

Click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

References: 1. EPCLUSA [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; July 2020. **2.** Lawitz E, Bourliere M, Han L, et al. Poster presented at: International Liver Congress; April 19-23, 2017; Amsterdam, Netherlands. **3.** Chhatwal J, Chen Q, Bethea ED, et al. The impact of direct-acting anti-virals on the hepatitis C care cascade: identifying progress and gaps towards hepatitis C elimination in the United States. *Aliment Pharmacol Ther*. 2019;50:66-74. **4.** Centers for Disease Control and Prevention. Viral hepatitis surveillance: United States, 2017. https://www.cdc.gov/hepatitis/statistics/2017surveillance/index.htm. Accessed Oct 14, 2019. **5.** US Preventive Services Task Force. Screening for hepatitis C virus infection in adolescents and adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2020;323(10):970-975. doi:10.1001/jama.2020.1123. **6.** Hepatitis C guidance 2018 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. AASLD-IDSA HCV Guidance Panel. *Clin Infect Dis*. 2018:67(10):1477-1492. **7.** Centers for Disease Control and Prevention. CDC recommendations for hepatitis C screening among adults – United States, 2020. https://www.cdc.gov/mmwr/volumes/69/rr/rr6902a1.htm?s_cid=r r6902a1_w. [Published April 9, 2020]. [Accessed June 6, 2020]. **8.** US Department of Health and Human Services, Center for Drug Evaluation and Research. Guidance for industry. Chronic hepatitis C virus infection: developing direct-acting antiviral drugs for treatment. [November 2017.] **9.** Grebely J, Dalgard O, Conway B, et al. Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *Lancet Gastroenterol Hepatol.* 2018;3(3):153-161. **10.** Rosenthal ES, Silk R, Mathur P, et al. Concurrent initiation of hepatitis C and opioid use disorder treatment in people who inject drugs. *Clin Infect Dis.* Published online February 3, 2020. doi: 10.1093/cid/ciaa105. **11.** Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med*. 2015;373(suppl):2599-2607. **12.** Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015;373(suppl):2608-2617. **13.** Liverpool Drug Interactions Group, University of Liverpool. Interactions charts for HCV DAAs and ribavirin. HEP Drug Interactions. [Updated March 2020]. [Accessed May 4, 2020]. https ://www.hep-druginteractions.org/prescribingresources.

GILEAD

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