Treatment of special populations: coinfection with HBV and HIV

Marina Roytman MD, FACP

Liver Program Director, UCSF Fresno

Clinical Professor, UCSF

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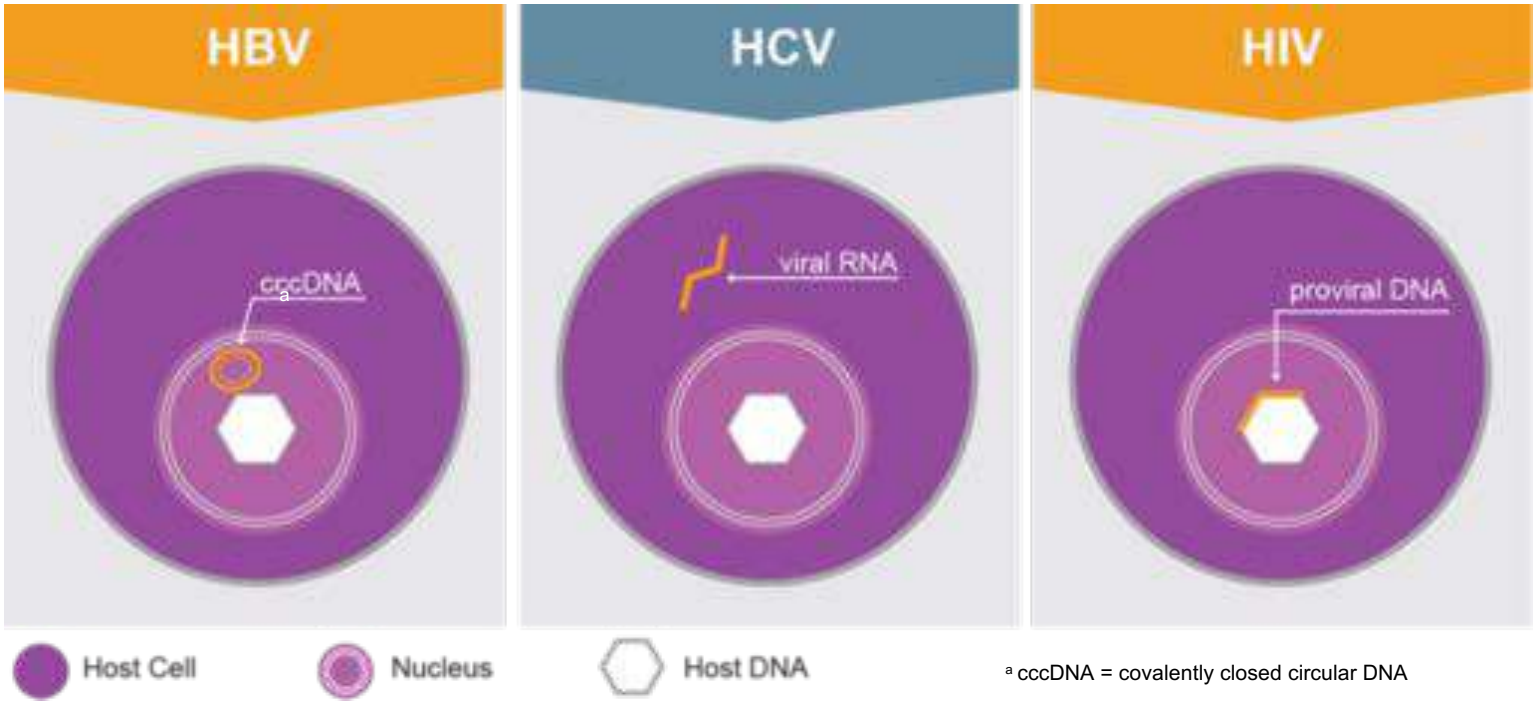
Why is HCV Curable?

- Unlike some other viruses, HCV RNA is only present in the cytoplasm (not in the nucleus) of the host cell[1]
- Without the stable, genetic-material reservoir of the nucleus created by other viruses, the possibility exists for HCV cure by treatment[1]



[a] cccDNA = covalently closed circular DNA

1. Soriano V, Perelson AS, Zoulim F. Why are there different dynamics in the selection of drug resistance in HIV and hepatitis B and C viruses? *J Antimicrob Chemother*. 2008;62(1):1-4.

Good News: Hepatitis B CDC Update

- Universal Hepatitis B screening:
  - at least once in a lifetime for all adults
  - Pregnant patients during each pregnancy
  - Triple panel testing

What is HBVr?

- Exacerbation of chronic HBV infection (HBsAg+)
  - ≥ 2 log increase in HBV DNA from baseline
  - >100 IU/cc in previously undetectable patient
- Reactivation of past HBV infection (HBsAg-, HBcAb+)
  - HBsAg- negative becomes HBsAg+
  - Appearance of HBV DNA
- Can lead to increased liver tests, liver failure and death

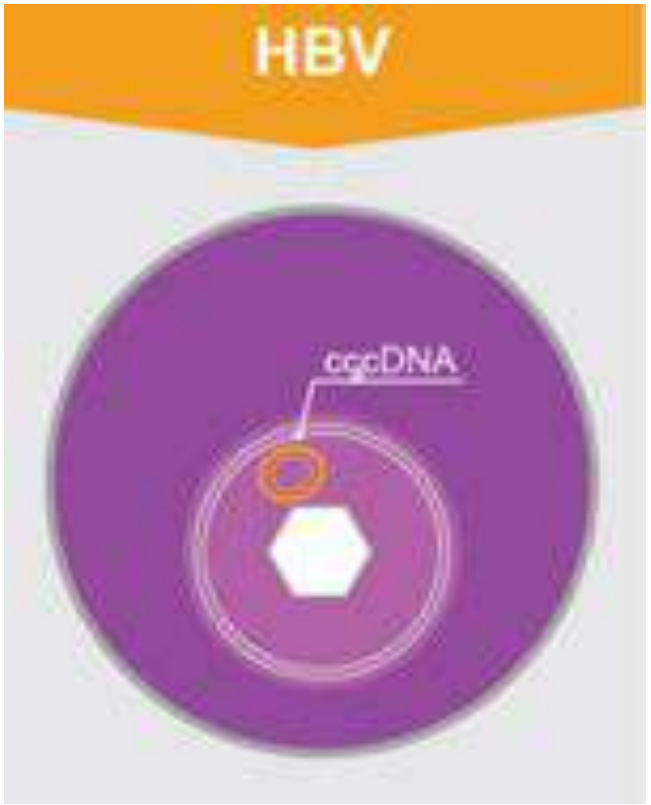
Hepatology International (2021) 15:1031-1048

Why does HBVr matter in HCV?

- Data from Asia-Pacific region:
  - 41% HBVr
  - 7% hepatitis flare
  - 2% mortality
- NOT associated with baseline HBV DNA level
- Associated with baseline quantitative HBsAg level
  - >10 IU/cc = 42.5% HBVr
  - <10 IU/cc = 18.5% HBVr

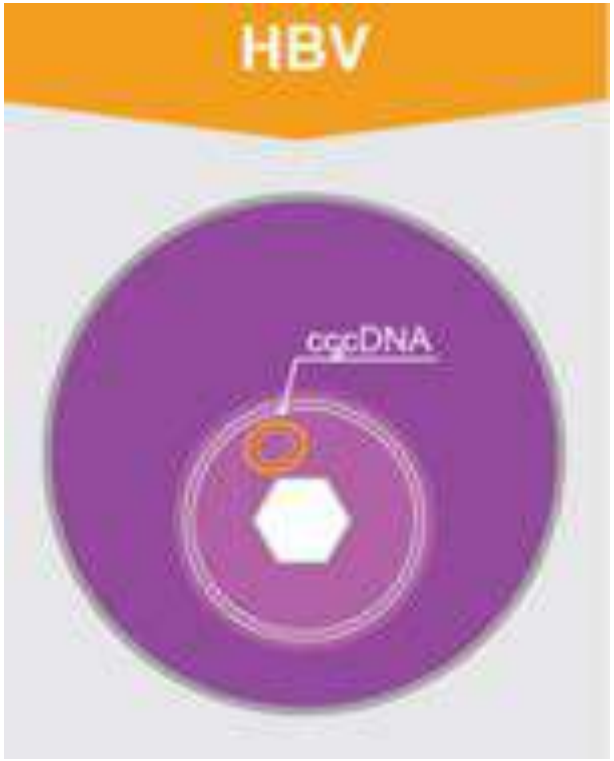
Who should be screened?

- All patients prior to HCV treatment!



What should be done for screening?

- Triple panel for all!
  - HBsAg = infection
    - HBV DNA
- HBcAb = exposure
- HBsAb = immunity



What determines risk of HBVr?

- Host factors
  - Older age, male sex, presence of cirrhosis, type of disease treated
- Virus factors
  - HBsAg+, high DNA levels, HBeAg+, absence of HBsAb+
  - Co-infection with HCV, HDV, HIV
- Concomitant use of immunosuppression

HCV-HBV dilemma

- Coincides with disappearance of HCV (weeks 4-8 of Rx)
- 24 cases internationally, post-marketing analysis
- Screen all HCV treatment candidates for HBV
- Treat all HBsAg+ patients until SVR12
- HBcAb +/- HBsAb: close ALT monitoring, reflex to DNA for unexpected elevations

Perillo RP. Hepatitis B Virus Reactivation During Direct-Acting Antiviral Treatment of Chronic Hepatitis C: A Hidden Danger of an Otherwise Major Success Story. HEPATOLOGY, VOL. 66, NO. 1, 2017

How should I manage and monitor my patient?

- It is mandatory and life-saving to start preemptive therapy in:
  - Patients with HBsAg+ with or without positive HBV DNA
  - Especially in patients with advanced fibrosis or cirrhosis!
- When in doubt: treat!

What medications should I use?

- TAF
- TDF
- Entecavir
- Preemptive start of treatment is more important than the choice of agent

HIV coinfection

- More liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality
- Associated with advanced liver fibrosis and cirrhosis in patients with HIV/HCV coinfection

Does simplified HCV treatment work for HIV coinfection?

- Yes!
- 399 patients Rx with SOF-VEL
  - 166 (42%) living with HIV = 94.6% SVR
  - 95.3% SVR without HIV

Solomon, Lancet Gastroenterol Hepatol. 2022;7(4):307-317

Can I use glecaprevir/pibrentasvir?

- Yes with the following drugs:
  - Abacavir, bictegravir, cabotegravir, dolutegravir, doravirine, emtricitabine, fostemsavir, ibalizumab-uiyk, lamivudine, maraviroc, raltegravir, rilpivirine, and tenofovir
- Yes with monitoring for hepatic toxicity:
  - Elvitegravir/cobicistat
- No with the following drugs:
  - Atazanavir, efavirenz, etravirine, nevirapine, or ritonavir-containing antiretroviral regimens

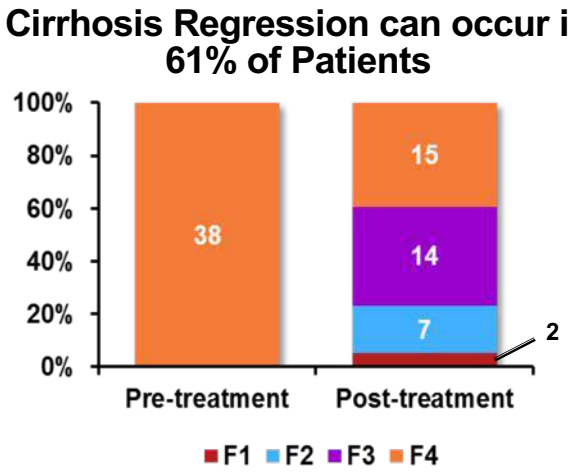
Can I use sofosbuvir/velpatasvir?

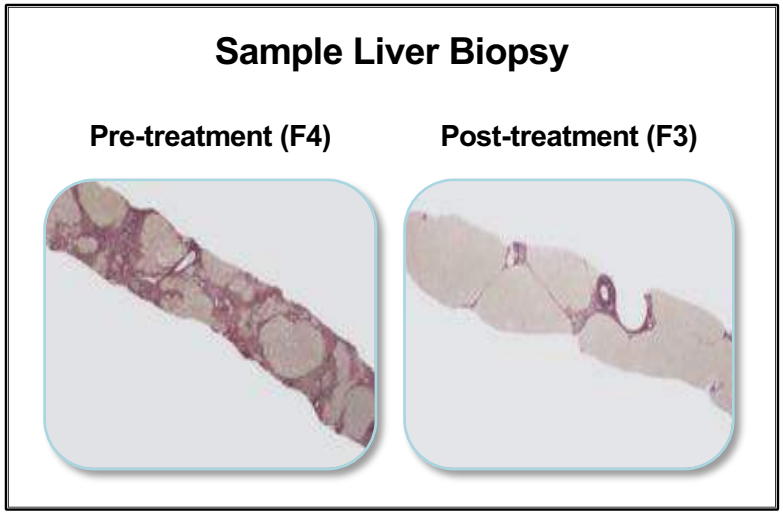
- Yes, with most antiretrovirals
- No with the following drugs:
  - Efavirenz, etravirine, tipranavir or nevirapine
- Monitor renal function in patients on TDF as part of HIV regimen
  - Avoid in patients with eGFR<60

Can I use sofosbuvir/velpatasvir/voxilaprevir?

- Yes with the following drugs:
  - Abacavir, bictegravir, cabotegravir, dolutegravir, doravirine, emtricitabine, ibalizumab-uiyk, lamivudine, maraviroc, raltegravir, rilpivirine, and tenofovir alafenamide.
- Yes with monitoring for hepatic toxicity:
  - Elvitegravir/cobicistat, darunavir/ritonavir
- No with the following drugs:
  - Efavirenz, etravirine, nevirapine, ritonavir-boosted atazanavir, tipranavir or ritonavir-boosted lopinavir
- Monitor renal function in patients on TDF as part of HIV regimen
  - Avoid in patients with eGFR<60

Cirrhosis Regression and Fibrosis Reduction Following SVR

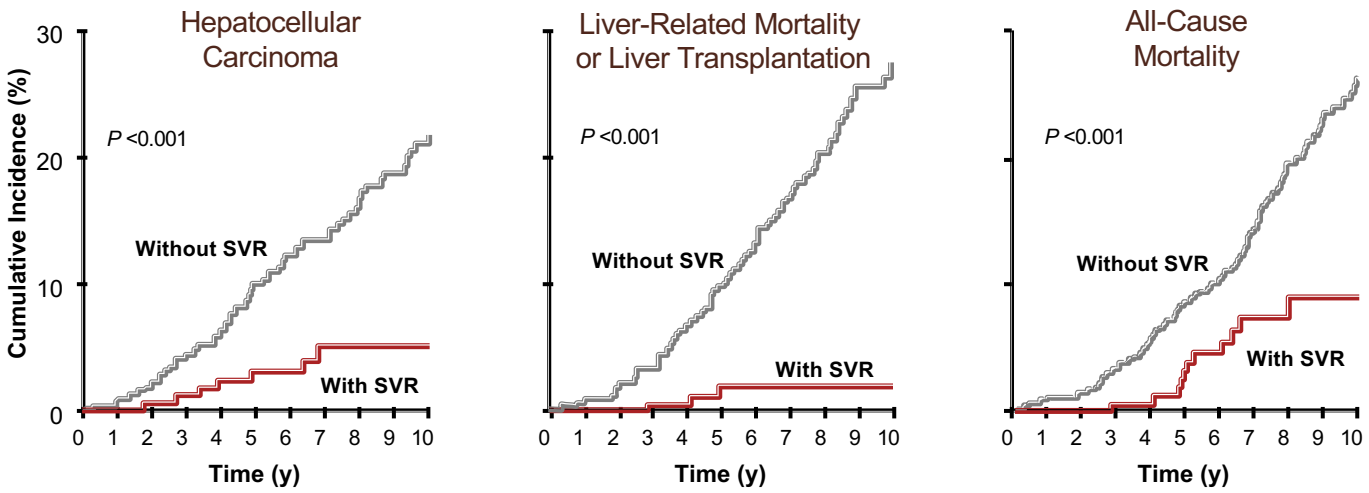




- **Fibrosis Reduction**
  - After treatment, the area of fibrosis decreased in 34/38 (89%) of patients
  - Post-treatment liver biopsies showed a significantly reduced area of fibrosis, with a median individual decrease of 71.8%

D'Ambrosio R, et al. *Hepatology*. 2012;56:532-543.

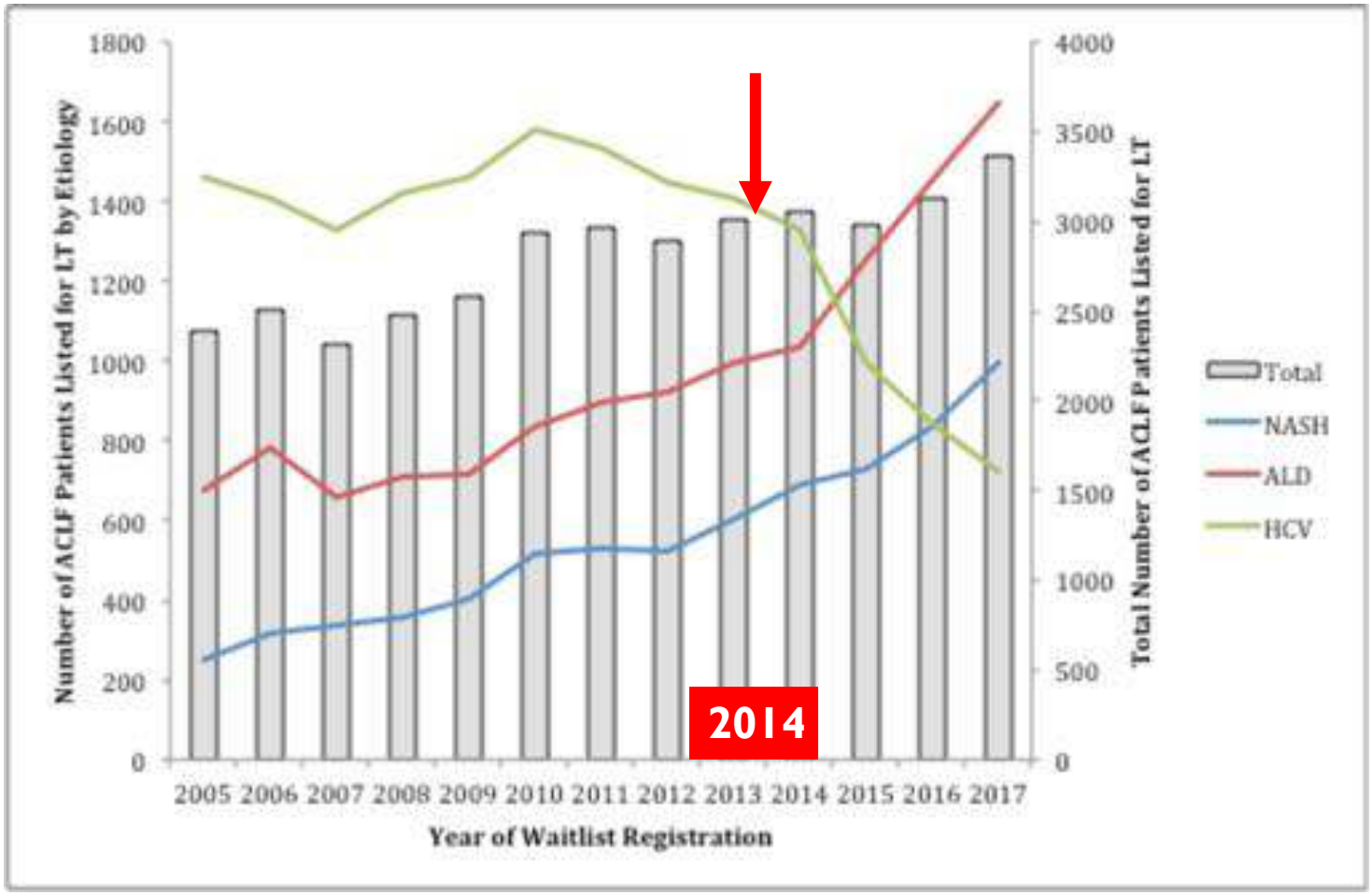
SVR Associated With a Reduction in HCC, Liver-Related Mortality, Transplantation, and All-Cause Mortality



- International, multicenter, long-term follow-up study of 530 consecutive CHC patients with advanced hepatic fibrosis or cirrhosis, who started an IFN-based treatment regimen between 1990 and 2003.
- Median follow-up duration 8.4 years
- Significant reduction of 10-year cumulative incidence of HCC, liver-related mortality or transplantation, and all-cause mortality in patients who achieved SVR

van der Meer AJ, et al. *JAMA*. 2012;308:2584-2593.

Trends in Liver Transplant Etiology of Acute on Chronic Liver Failure: UNOS Registry



In 2017 ALD was the leading etiology nationally, among listed patients with ACLF (n=1649), followed by NASH (n=998), then HCV (n=720)

V. Sundaram et al. Hepatology 2019 #1072

Congratulations!
Today is your day!
You're off to Great Places!
You're off and away!

Dr. Seuss

Everyone should know their ABCs of Hepatitis!

A

HAV ab total
=
immunity

B

HBsAb = immunity
HBsAg = infection
HBcAb total =
exposure

C

HCV Ab
=
infection