Project ECHO®

Hawai`i Learning Groups

Hepatitis and Liver Health ECHO

HIV and HCV Co-Infection

April 9, 2021

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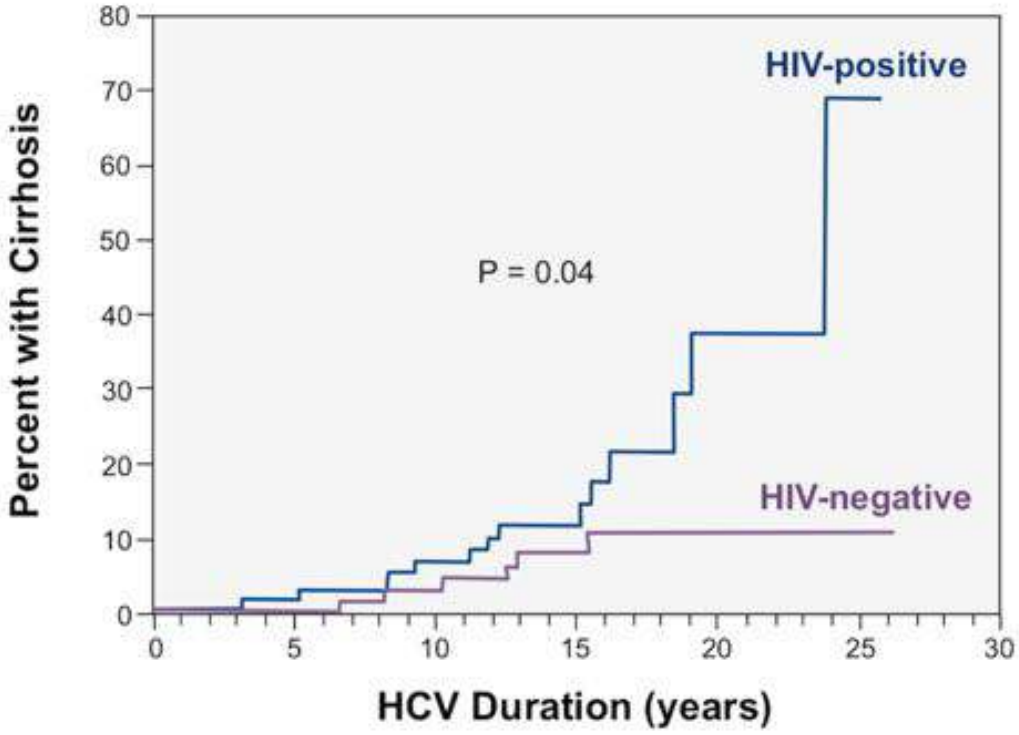
Epidemiology

- Among persons living with HIV in the United States, an estimated 15 to 30% have HCV coinfection
- Coinfection accelerates the progression of hepatic fibrosis and more aggressive course of liver disease



Source: Di Martino V, Rufat P, Boyer N, et al. The influence of human immunodeficiency virus coinfection on chronic hepatitis C in injection drug users: a long-term retrospective cohort study. Hepatology. 2001;34:1193-9.

Epidemiology

- Cirrhosis has been observed to occur 12 to 16 years earlier in HCV/HIV co-infection compared with those who have HCV monoinfection
- Liver-related deaths in persons living with HIV are attributable to HCV infection
- Limited access to liver transplantation
- Treatment of HCV in persons with HIV coinfection remains a high priority

SVR Rates with GT 1 HCV-HIV Coinfection and HCV Monoinfection				
Regimen (12 weeks)	Genotype 1			
	HCV-HIV Coinfection		HCV Monoinfection	
	Study	SVR	Study	SVR
Elbasvir-Grazoprevir	C-EDGE Coinfection	95%	C-EDGE TN	95%
Glecaprevir-Pibrentasvir	EXPEDITION-2	98%	ENDURANCE-1	99%
Ledipasvir-Sofosbuvir	ION-4	96%	ION-1	99%
Sofosbuvir-Velpatasvir	ASTRAL-5	95%	ASTRAL-1	98%

- Direct-acting antiviral (DAA)-based therapy have demonstrated SVR rates in HIV-HCV coinfection comparable to those with HCV monoinfection
- No longer should be considered as a “treatment-refractory” population
- In these trials, most participants did not have cirrhosis and most had CD4 counts > 200 cells/mm^3

https://www.hepatitisc.uw.edu/go/key-populations-situations/treatment-hiv-coinfection/core-concept/all

Cotreatment of HCV and HIV Coinfection: Factors to Consider

- **HCV workup if starting DAA**
  - HCV Genotype
  - HCV RNA level
  - Staging of liver disease
    - Child-Pugh score
    - Endoscopy?
    - HCC screening
  - Previous DAAs, potential need for resistance testing
  - HBV status

- **HIV workup if starting/switching ART**
  - HIV-1 RNA level
  - HLA*B-5701 status
  - CD4+ cell count
  - Resistance testing
- **All patients**
  - CrCl
  - Non-ART, non-DAA comedications
    - PPIs
    - Statins
    - Antiseizure drugs
    - Herbal supplements
  - Comorbidities

AASLD/IDSA HCV Guidelines.

Slide credit: clinicaloptions.com

HCV DAAs Target Steps of HCV Life Cycle

Inhibitor Class	Suffix	Examples
Targeting HCV Protein Processing		
NS3/4 Protease[1]	-PREVIR	▪ Glecaprevir, grazoprevir, paritaprevir, simeprevir, voxilaprevir
Targeting HCV Protein Processing		
NS5B Polymerase[2]	-BUVIR	▪ Nucleotide: sofosbuvir ▪ Nonnucleoside: dasabuvir
NS5A[3]	-ASVIR	▪ Daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir

1. McCauley JA, et al. Curr Opin Pharmacol. 2016;30:84-92.
2. Eltahla AA, et al. Viruses. 2015;7:5206-5224.
3. Gitto S, et al. J Viral Hepat. 2017;24:180-186.

Slide credit: clinicaloptions.com

AASLD/IDSA Recommendations for First-line HCV Treatment in HCV/HIV Coinfection

Regimen by HCV GT	Duration, Wks	No Cirrhosis	Compensated Cirrhosis‡	eGFR < 30 mL/min
1, 4	8	GLE/PIB (MAVYRET)	–	GLE/PIB‡‖
	12	GZR/EBR (ZEPATIER)* SOF/LDV (HARVONI)† SOF/VEL (EPCLUSA)	GLE/PIB, GZR/EBR,* SOF/LDV, SOF/VEL	GZR/EBR
2, 3	8	GLE/PIB (MAVYRET)	–	GLE/PIB‡‖
	12	SOF/VEL (EPCLUSA)	GLE/PIB, SOF/VEL§	–
5, 6	8	GLE/PIB (MAVYRET)	–	GLE/PIB‡‖
	12	SOF/LDV (HARVONI) SOF/VEL (EPCLUSA)	GLE/PIB, SOF/LDV, SOF/VEL	–

All options available QD

*If GT1a with BL NS5A RASs for EBR, 12 wks not recommended; can increase duration to 16 wks with RBV (alternative).

†Some data to support 8 wks in GT1, but 8 wks not recommended in HCV/HIV coinfection.

‡If decompensated cirrhosis, do not use HCV protease inhibitors.

§If BL Y93H RAS present in GT3, add RBV or consider SOF/VEL/VOX.

‖If also cirrhotic, increase duration to 12 wks.

AASLD/IDSA HCV Guidelines.

Slide credit: clinicaloptions.com

DHHS Guidelines: Recommended Regimens for First-line ART

Class	Regimen
INSTI	▪ **BIC/TAF/FTC** ▪ **DTG/ABC/3TC** ▪ DTG + (TAF or TDF)/FTC ▪ **EVG/COBI/(TAF or TDF)/FTC** ▪ RAL + (TAF or TDF)/FTC

Bold text identifies single-tablet regimens.

- Recommendations may differ based on BL HIV-1 RNA, CD4+ cell count, CrCl, eGFR, HLA-B*5701 status, HBsAg status, osteoporosis status, and pregnancy status
- All options available QD (except in pregnancy)

DHHS Guidelines. 2020.

Slide credit: clinicaloptions.com

HIV/HCV Drug–Drug Interactions

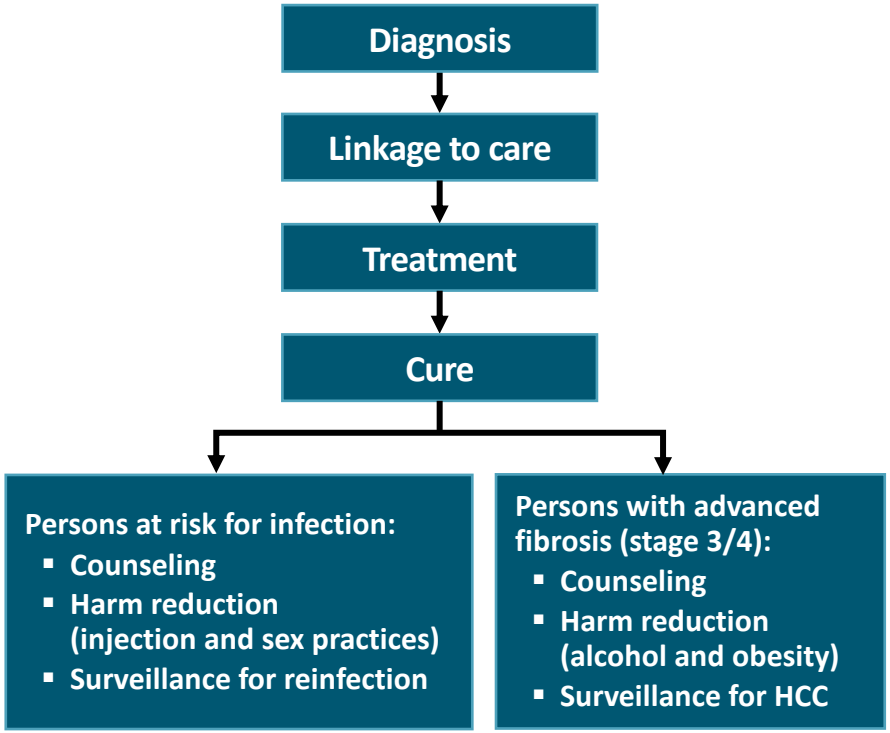
ARV(s)	GLE/PIB	GZR/EBR	SOF/LDV	SOF/VEL	SOF/VEL/VOX
ATV + (RTV or COBI)	X	X	✓*	✓*	X
DRV + (RTV or COBI)	X	X	✓*	✓*	✓*†‡
LPV + RTV	X	X	✓*	✓*	X
EFV	X	X	✓*	X	X
RPV	✓	✓	✓*	✓	✓
BIC	–§	–§	✓†	✓†	✓†
DTG	✓	✓	✓*	✓	✓
RAL	✓	✓	✓	✓	✓
EVG/COBI/FTC/TDF	✓*†	X	X	✓*	✓*†
EVG/COBI/FTC/TAF	✓†	X	✓	✓	✓†
3TC/ABC	✓	✓	✓	✓	✓
TAF or TDF	✓	✓	✓*	✓*	✓*

*Monitor for tenofovir toxicity if used with TDF. †No clinically significant drug interaction per prescribing information. ‡Guidelines recommend monitoring liver enzymes owing to lack of clinical safety data. §No information in prescribing information.

DHHS Guidelines. 2018.

Slide credit: clinicaloptions.com

HCV Care Continues Past Achievement of SVR



Characteristic	Follow up After SVR
No advanced fibrosis (Metavir stage F0-F2), no or low risk of HCV reinfection	▪ Standard medical care, as in someone without HCV
Advanced fibrosis (Metavir stage F3 or F4)	▪ Ultrasound surveillance for HCC every 6 mos ± AFP
Moderate to high risk of HCV reinfection	▪ Harm reduction ▪ HCV RNA every 12 mos

Falade-Nwulia O, et al. J Hepatol. 2017;66:267-269. AASLD/IDSA HCV Guidelines.

Slide credit: clinicaloptions.com

Summary

- As HCV/HIV coinfected individuals have more rapid progression to advanced liver disease, HCV therapy is a priority
- All co-infected individuals should be treated with potent ART, preferably with INSTI
    - Goal of HIV virologic suppression prior to HCV therapy
- Switching HIV antiretroviral medications may be indicated depending on the situation and history of HIV antiretroviral resistance
- HCV antiviral regimen selection is generally the same as for HCV monoinfection
    - Regimen selection based on genotype, history of prior HCV treatment, stage of liver fibrosis and potential drug interaction between ART and HCV antiviral medications
- Continual monitoring for HCC for advanced fibrosis
- Screening for reinfection is essential in high-risk groups

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