Hepatitis and Liver Health ECHO

HIV and HCV Co-Infection

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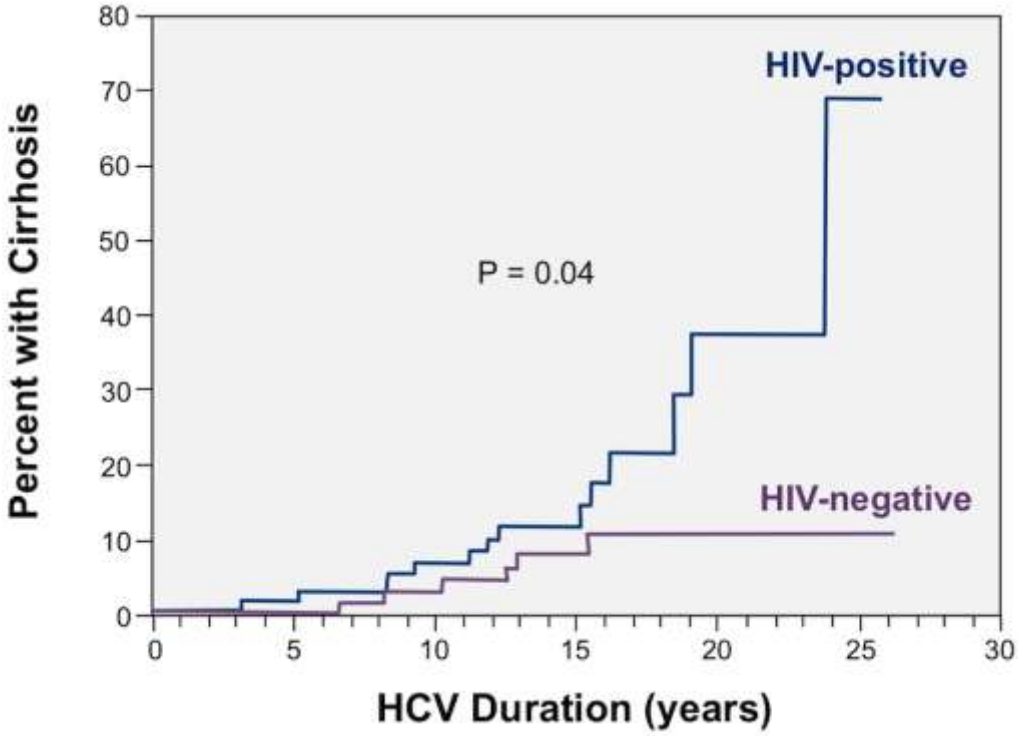
Epidemiology

- 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

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AASLD/IDSA HCV Guidelines.

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

HCV GT	Duration, Wk	HCV Regimen	
		No Cirrhosis	Compensated Cirrhosis‡
1, 4	8	GLE/PIB (MAVYRET)	–
	12	EBR/GZR (ZEPATIER)*, LDV/SOF (HARVONI)†, SOF/VEL (EPCLUSA)	GLE/PIB, EBR/GZR,* LDV/SOF, SOF/VEL
2, 3	8	GLE/PIB	–
	12	SOF/VEL	GLE/PIB, SOF/VEL§
5, 6	8	–	–
	12	GLE/PIB, LDV/SOF, SOF/VEL	GLE/PIB, LDV/SOF, SOF/VEL

*Alternative option; if GT1a with BL NS5A RASs for EBR, 12 wk not recommended; can increase duration to 16 wk with RBV. †Some data to support 8 wk in GT1, but 8 wk 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.

AASLD/IDSA HCV guidelines. 2021.

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

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	–

*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

HIV/HCV Drug–Drug Interactions

No interaction expected | Potential interaction | Do not coadminister

Recommended First- and Second-line ARVs	EBR/GZR	GLE/PIB	LDV/SOF	SOF/VEL	SOF/VEL/VOX
ATV + (RTV or COBI)	X	X	✓*	✓*	X
DRV + (RTV or COBI)	X	X	✓*	✓*	✓*†
DOR	✓	✓	✓	✓	✓
EFV	X	X	✓*	X	X
RPV	✓	✓	✓*	✓	✓
BIC	✓	✓	✓	✓	✓
DTG	✓	✓	✓	✓	✓
RAL	✓	✓	✓	✓	✓
EVG/COBI/FTC/TDF	X	✓*†	X	✓*	✓*†
EVG/COBI/FTC/TAF	X	✓†	✓	✓	✓†
3TC or FTC or ABC	✓	✓	✓	✓	✓
TAF or TDF	✓	✓	✓‡	✓‡	✓‡

*Monitor for tenofovir toxicity in combination with TDF. †Consider monitoring for hepatotoxicity. ‡Monitor for tenofovir toxicity with TDF.

DHHS. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV.

Slide credit: clinicaloptions.com

International Guidance on First-line ART

DHHS[1]	IAS-USA[2]	EACS[3]	WHO[4]
Recommended Initial Regimens for Most PWH ▪ BIC/FTC/TAF ▪ DTG/ABC/3TC* ▪ DTG + XTC + (TAF or TDF) ▪ DTG/3TC†	*Recommended Initial Regimens for Most PWH* ▪ BIC/FTC/TAF ▪ DTG + FTC/TAF or XTC/TDF ▪ DTG + 3TC†‡	*Recommended* ▪ BIC/FTC/TAF ▪ DTG/ABC/3TC* ▪ DTG + FTC/TAF or XTC/TDF ▪ RAL + FTC/TAF or XTC/TDF ▪ DTG + 3TC§ ▪ DOR + FTC/TAF or XTC/TDF or DOR/3TC/TDF	*Recommended* ▪ DTG + XTC/TDF *Alternative* ▪ EFV + 3TC + TDF

*Only if HLA-B*5701 negative. †Except when HIV-1 RNA >500,000 copies/mL, HBV coinfected, or ART to be started before RT genotypic resistance testing or HBV testing results available. ‡"Perhaps" not recommended for patients with a CD4+ cell count <200 cells/mm^3. §Only if HBsAg negative and HIV-1 RNA <500,000 copies/mL.

1. DHHS. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV.
2. Saag. JAMA. 2020;324:1651. 3. EACS Guidelines v11.0, October 2021. 4. who.int/publications/i/item/9789240031593.

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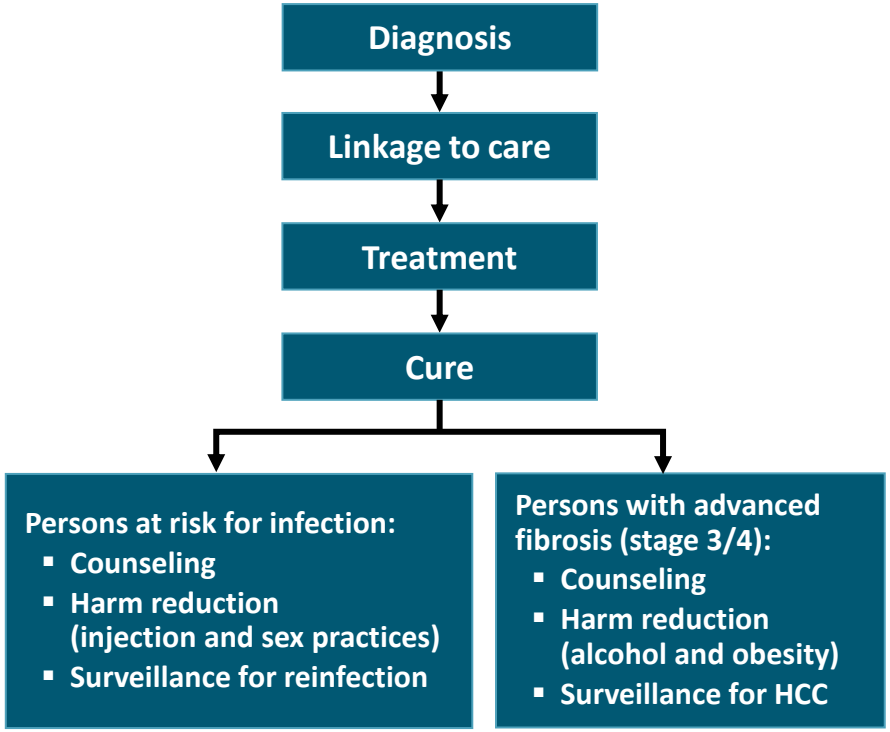
HCV Care Continues Past Achievement of SVR



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

Acknowledgements

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Clinical Care Options

MAHALO

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