CLINICAL CARE OPTIONS®
HEPATITIS

Insights in Managing Patients With HCV/HIV Coinfection

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Treatment of HCV and HIV Infection in Persons With Coinfection

- All persons with HIV should be treated with **potent ART,** especially those with HIV/HCV coinfection[1]
  - HIV infection is independently associated with HCV disease progression[2]
- **HCV treatment** should also be a priority for persons with HCV/HIV coinfection[2]
  - Efficacy and adverse event rates of HCV DAAs among those with HCV/HIV coinfection are similar to those observed with HCV alone
  - Cotreatment "requires continued awareness and attention to the complex drug–drug interactions that can occur between DAAs and antiretroviral medications"

1. DHHS Guidelines. 2018. 2. AASLD/IDSA HCV Guidelines. 2017.

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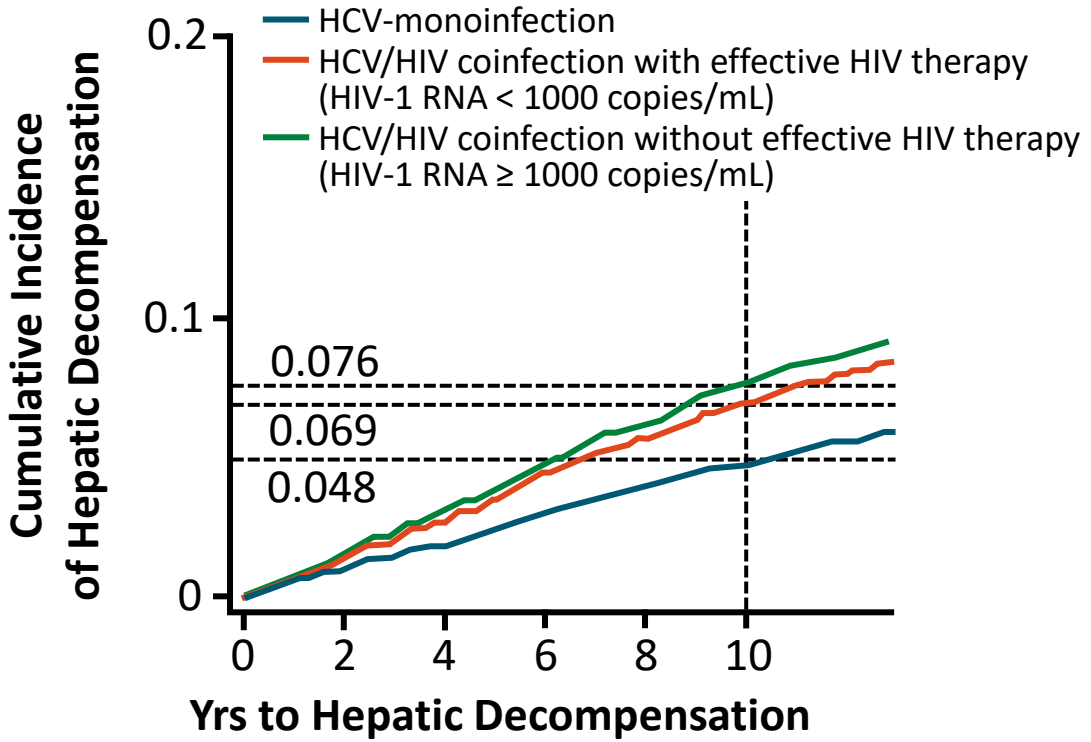
Disease Progression in HCV Monoinfection vs HCV/HIV Coinfection With or Without HIV Suppression

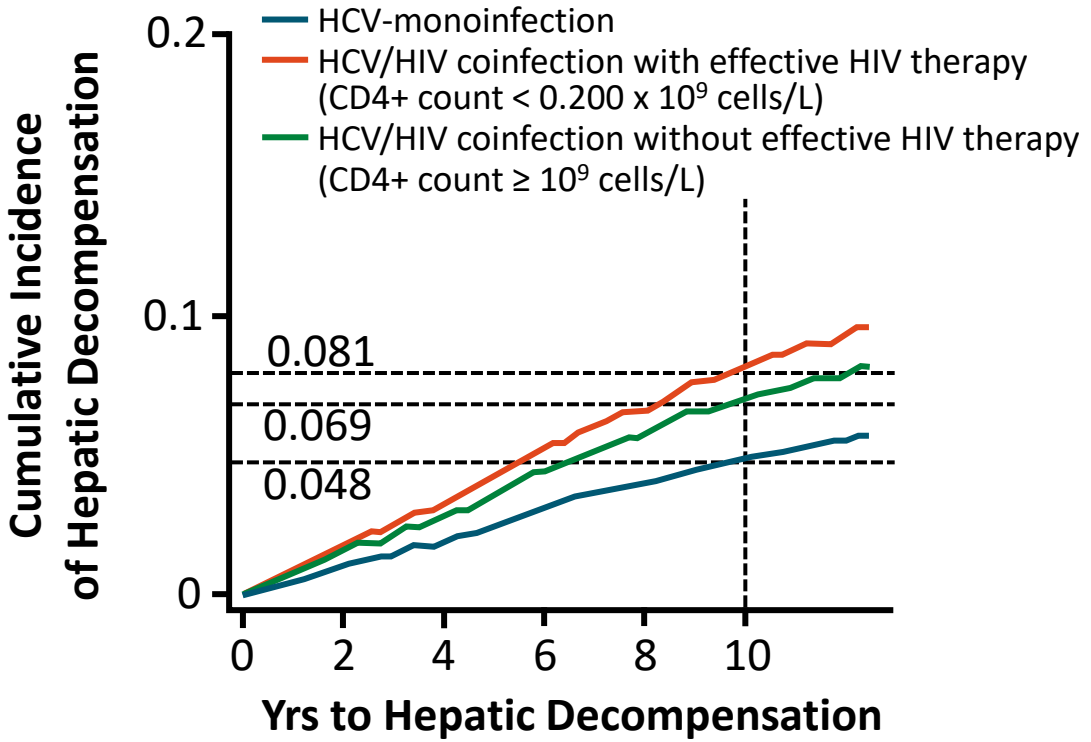
- Retrospective cohort study of HCV-infected, treatment-naive patients in the Veterans Health Administration (N = 10,359)

Time to Decompensation by Maintained HIV RNA Level



- If HIV-1 RNA < 1000 copies/mL: +65% excess risk
- If HIV-1 RNA ≥ 1000 copies/mL: +82% excess risk

Time to Decompensation by Maintained CD4+ Cell Count



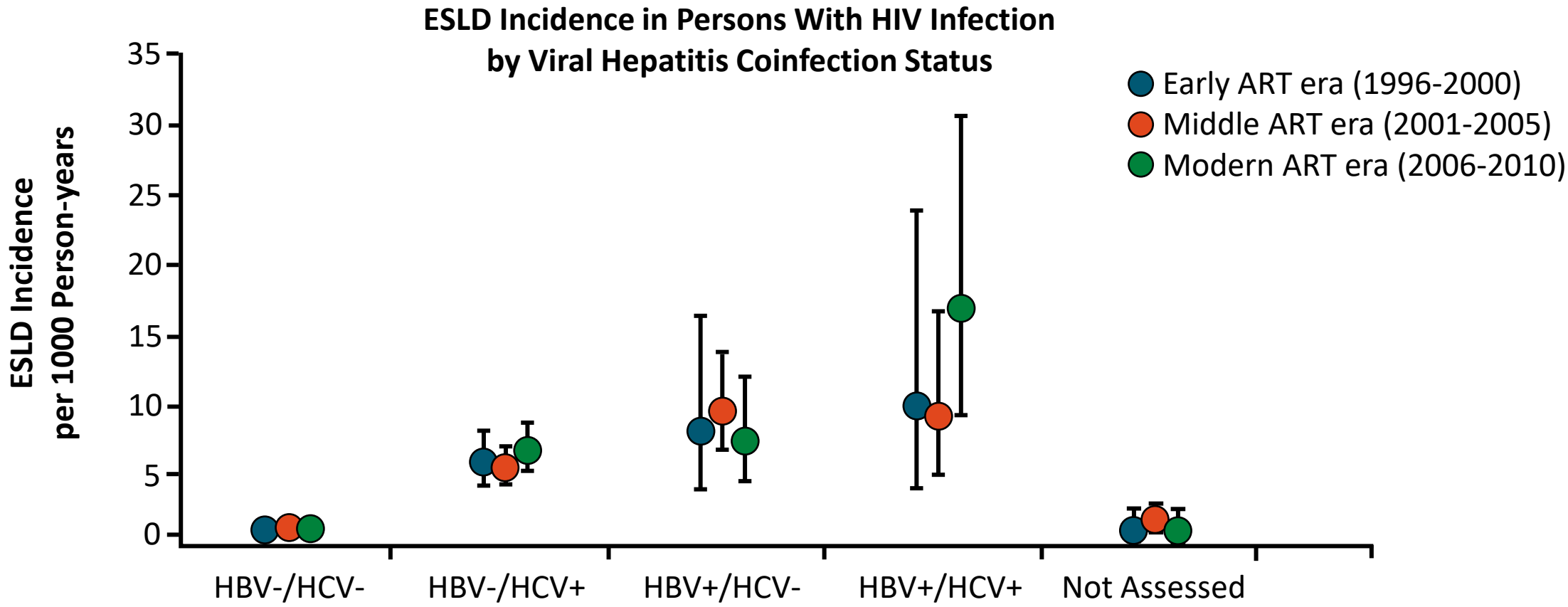
- If CD4+ < 200/mm^2: +203% excess risk
- If CD4+ ≥ 200/mm^2: +56% to 63% excess risk

Lo Re III V, et al. Ann Intern Med. 2014;160:369-379.

Slide credit: clinicaloptions.com

No Decline in ESLD Incidence in Persons With HCV/HIV Coinfection in the Modern ART Era

- 34,119 HIV-infected adults followed for 129,818 person-yrs; 380 incident ESLD outcomes occurred



Klein MB, et al. Clin Infect Dis. 2016;63:1160-1167.

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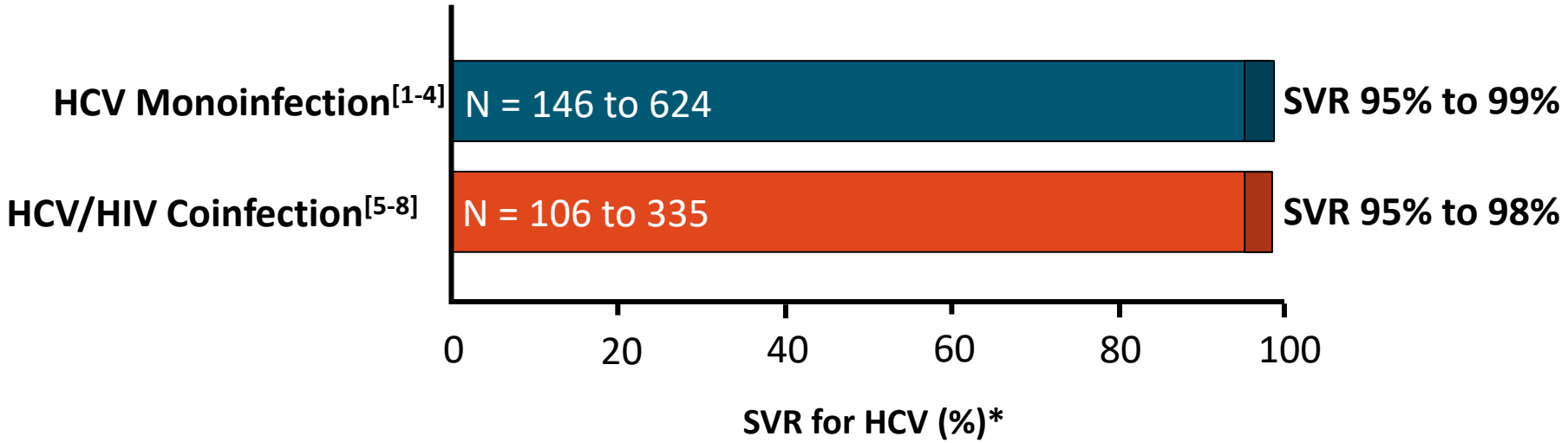
HCV DAAs Have Similar Efficacy in Persons With and Without HIV Coinfection

Efficacy Across Separate Phase III Studies of GT1-6 HCV Infection With GLE/PIB, GZR/EBR, SOF/LDV, or SOF/VEL



*Most data reported for these studies are from treatment-naive patients with GT1/4 HCV infection receiving 12-wk regimens.

References in slidenotes

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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.

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	–	GLE/PIB‡
	12	GZR/EBR,* SOF/LDV,† SOF/VEL	GLE/PIB, GZR/EBR,* SOF/LDV, SOF/VEL	GZR/EBR
2, 3	8	GLE/PIB	–	GLE/PIB‡
	12	SOF/VEL	GLE/PIB, SOF/VEL§	–
5, 6	8	GLE/PIB	–	GLE/PIB‡
	12	SOF/LDV, SOF/VEL	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. 2017.

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[2] (except in pregnancy)

1. DHHS Guidelines. 2018. 2. Raltegravir [package insert]. 2018.

Slide credit: clinicaloptions.com

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
  - Comorbidities

1. AASLD/IDSA HCV Guidelines. 2017.

Slide credit: clinicaloptions.com

Common Scenarios for the Cotreatment of HCV and HIV Infection

1. Persons taking ART with HIV RNA suppression who plan to initiate HCV DAA therapy

- Decisions:
  - Selection of HCV DAA regimen
  - Adjustment of ART to facilitate a specific DAA regimen

2. Persons not taking ART who plan to initiate HCV DAA therapy

- Decision:
  - Which infection to treat first, or whether to start both treatments simultaneously

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Case 1: Stable ART initiating HCV DAA therapy

A 58-yr-old man with HIV and chronic HCV infection

- **HIV**
  - Stable on initial regimen of ATV/RTV + 3TC + TDF
  - HIV-1 RNA < 20 copies/mL
  - CD4+ cell count 800 cells/mm^3
  - HLA-B*5701 negative
- **HCV**
  - Treatment-naive GT1a
  - HCV RNA 1.43 million IU/mL
    - No NS5A RASs
  - Liver stiffness = 8.8 kPa (~ F2)
  - eGFR = 65 mL/min
  - HBsAg negative

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

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	✓	✓	✓*	✓*	✓*

Coadministration of HCV and HIV PIs not currently recommended

*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

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			
EVG/COBI/FTC/TAF	✓†	X	✓		✓†
3TC/ABC	✓	✓	✓		✓
TAF or TDF	✓	✓	✓*	✓*	✓*

Coadministration of LDV or VEL with TDF, but not TAF, requires liver monitoring

*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

Principles of ART Regimen Switching in Virologically Suppressed Patients

- Review ART history for previous intolerance or HIV virologic failure
- Review HIV resistance test results
- If previous HIV resistance uncertain, consider a switch only if new regimen likely to maintain suppression of resistant virus
- In patients with HBV/HIV coinfection, continue ARVs active against HBV (even if not needed for HIV suppression)
  - (TAF or TDF) plus (3TC or FTC)
- Check HIV-1 RNA during first 3 mos after switch to ensure suppression
- Monotherapy with boosted PI or INSTI not recommended

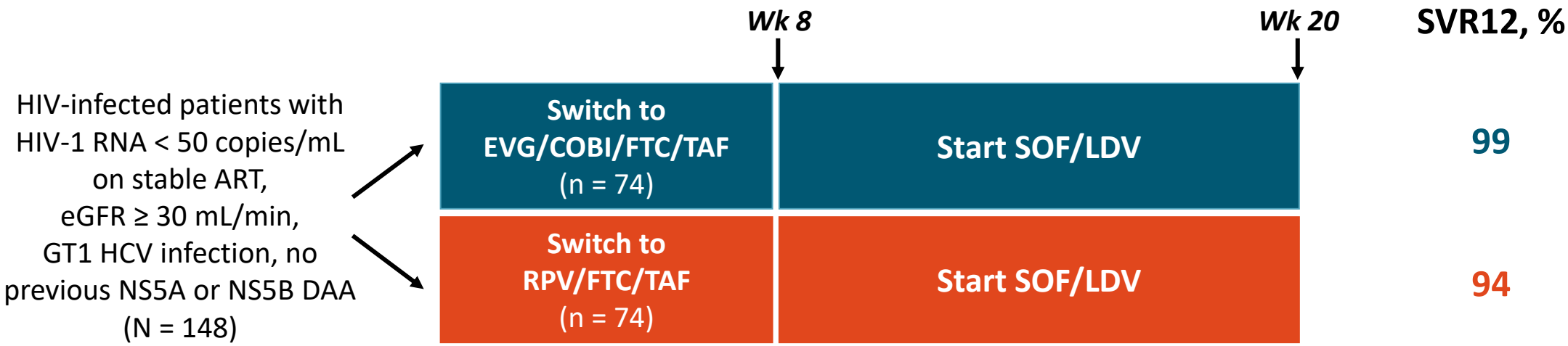
My approach: Consider ≥ 4-wk adjustment before starting HCV DAAs to ensure ART is tolerated and effective

DHHS Guidelines. 2018.

Slide credit: clinicaloptions.com

GS-1992: SOF/LDV in HIV/HCV Coinfection After Switch to TAF-Based Regimens

- Randomized, open-label phase IIIb trial



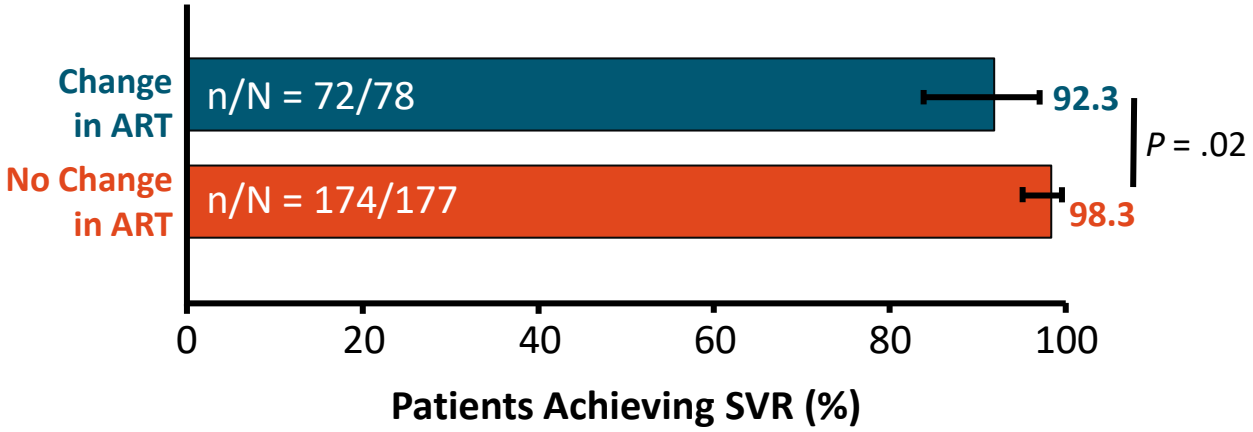
- Switch to TAF-based regimen maintained HIV-1 RNA < 50 copies/mL in 95% of patients
  - D/C before Wk 8 for lack of efficacy (n = 1), no resistance to ART

Ramgopal M, et al. AASLD 2017. Abstract LB-12. ClinicalTrials.gov. NCT02707601.

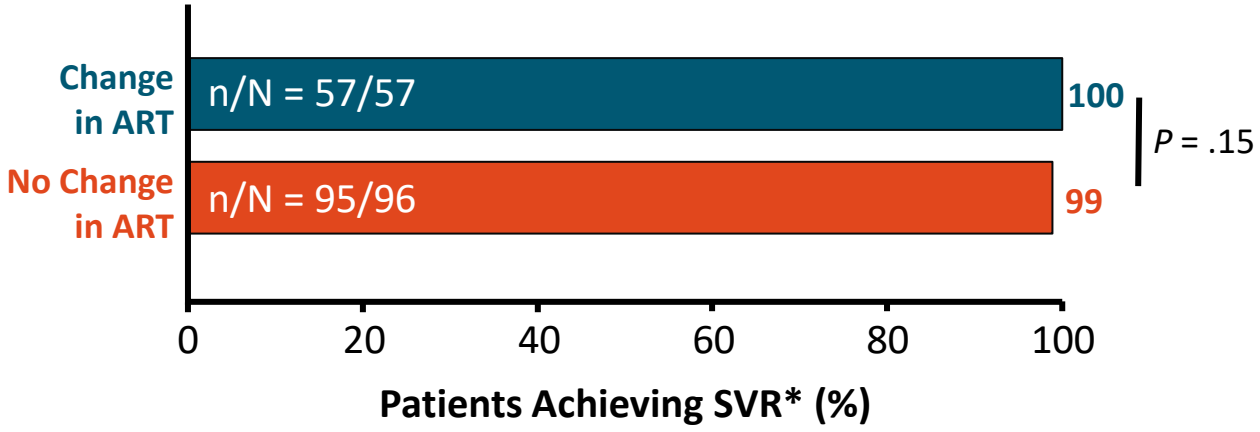
Slide credit: clinicaloptions.com

Does Switching ART Affect Likelihood of HCV Cure?

- Real-world, single-center cohort study of HCV/HIV-coinfected patients treated with DAAs (N = 255)[1]



- Observational, multicenter, 3-year study of HCV/HIV coinfected patients treated with SOF/LDV (N = 166)[2]



*In subgroup of N = 153 where SVR was reported.

1. Falade-Nwulia O, et al. Hepatology. 2017;66:1402-1412. 2. Marks K, et al. CROI 2018. Abstract 604

Consider Potential for HBV Reactivation

- Test all patients initiating HCV DAA therapy for HBsAg, anti-HBc, and anti-HBs[1]
- **HIV-infected patients with active HBV infection (HBsAg positive)** should receive dual NRTI therapy with anti-HBV activity[2]
  - (TAF or TDF) plus (3TC or FTC), or entecavir if TAF or TDF not feasible
  - Initiate ART before DAA therapy owing to risk of HBV reactivation with DAAs
- **In patients positive for anti-HBc ± anti-HBs,[1]** no consensus on approach
  - Risk of HBV reactivation is very low,[3] but consider monitoring transaminases at Wks 4 and 8 following HCV DAA initiation
  - Insufficient data to inform HBV DNA monitoring

1. AASLD/IDSA HCV Guidelines. 2017.
2. DHHS Guidelines. 2017.
3. Belperio PS, et al. Hepatology. 2017;66:27-36.

Case 2: Cotreatment of both HIV and HCV infection

- A 38-year-old man with HIV and HCV infection who has re-established care
  - Injection heroin use; currently in a residential medication-assisted therapy program
  - eGFR 55 mL/min
- **HIV**
  - Out of care; previous HIV treatment with EFV/TDF/FTC
  - CD4+ count 385 cells/mm^3 and HIV RNA 54,340 copies/mL
  - HLA-B*5701 negative
- **HCV**
  - HCV genotype 3a infection with HCV RNA = 1.5 million IU/mL
  - Liver elastography consistent with stage 3 fibrosis
  - HBsAg negative

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	–	GLE/PIB‖
	12	GZR/EBR,* SOF/LDV,† SOF/VEL	GLE/PIB, GZR/EBR,* SOF/LDV, SOF/VEL	GZR/EBR
2, 3	8	GLE/PIB	–	GLE/PIB‖
	12	SOF/VEL	GLE/PIB, SOF/VEL§	–
5, 6	8	GLE/PIB	–	GLE/PIB‖
	12	SOF/LDV, SOF/VEL	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 HIV/HCV 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. 2017.

Slide credit: clinicaloptions.com

Cotreatment of HIV and HCV coinfection

- For many patients, initiation of ART should be prioritized; however, HIV treatment and HIV-1 RNA suppression are not required before HCV DAAs
  - Treatment readiness for 8-12 wks of HCV DAAs may be different than for lifelong ART
  - HCV treatment and cure may serve to facilitate HIV care engagement
  - SVR may reduce the risk of drug-induced liver injury
- If ART is initiated first, consider delaying HCV DAAs for 4-6 wks to confirm tolerability and HIV-1 RNA response

AASLD/IDSA HCV Guidelines. 2017.

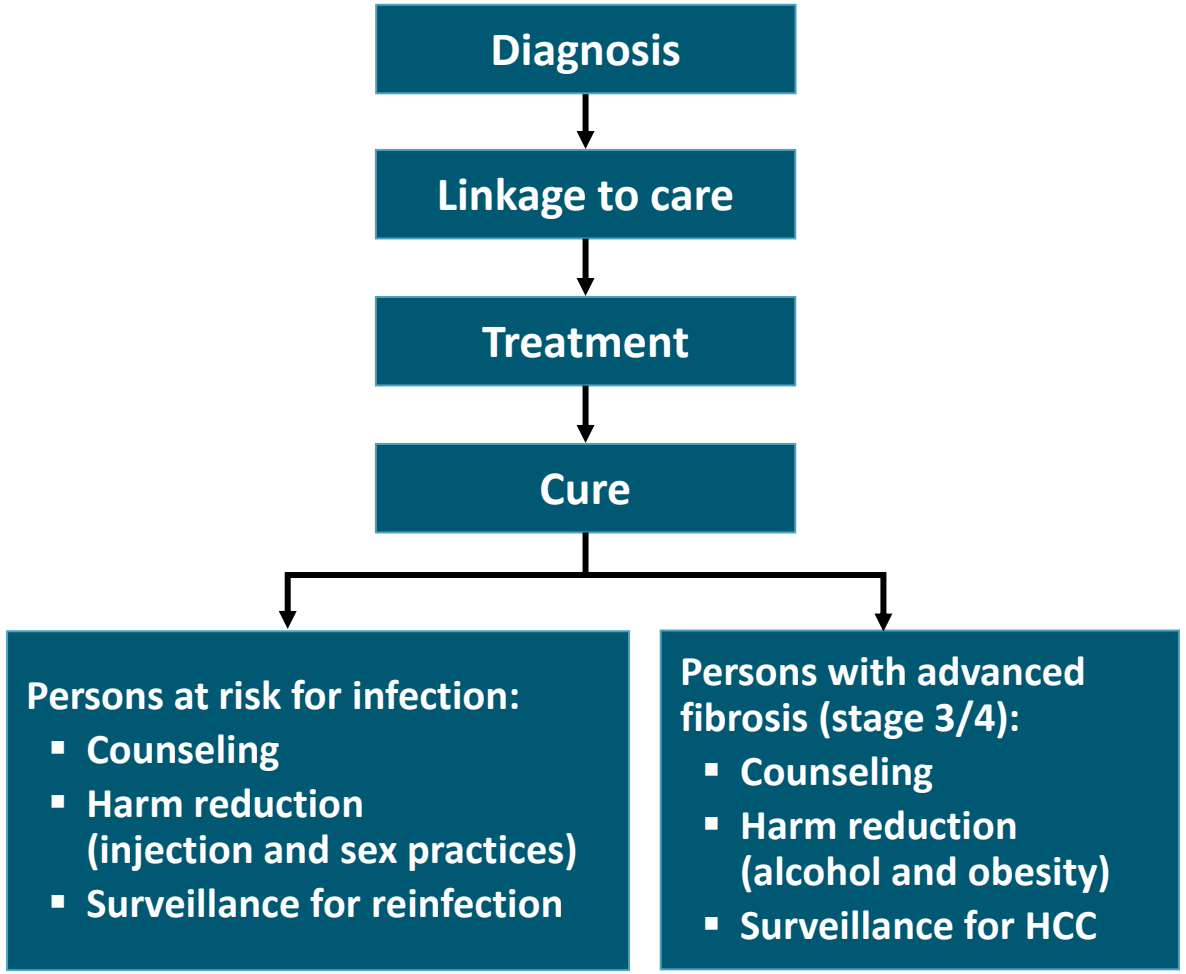
Slide credit: clinicaloptions.com

Common DDIs With Non-ART, Non-DAA Comedications

- PPIs
- Statins
- Antiseizure drugs
  - Carbamazepine
  - Phenytoin
- Herbals (St John's wort)
- Over-the-counter medications (including antacids)

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. 2017.

Slide credit: clinicaloptions.com

Summary: Treatment of HCV and HIV Infection in Persons With Coinfection

- All persons with HIV should be treated with potent ART, especially those with HCV
  - Despite ART, HIV infection is independently associated with HCV disease progression

What do the guidelines recommend for HCV/HIV coinfection in patient scenarios that *you* specify?

See our simple tool: **Guidance on Cotreatment of HCV and HIV Infection**

- HCV treatment should also be a priority for persons with HCV/HIV coinfection
  - Efficacy and adverse event rates for HCV DAAs among those with HCV/HIV coinfection are similar to those observed with HCV alone
  - Cotreatment requires continued awareness and attention to the complex DDIs that can occur between DAAs and ARV medications

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CME/CE-certified Clinical Focus Module reviewing key data and guideline-based management strategies

Online Interactive Treatment Decision Tool providing tailored guidance on selecting treatments for your patients with HCV/HIV coinfection

ClinicalThought commentaries from expert faculty

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