# Cases: Initial Treatment of Hepatitis C

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IAS–USA

## Off-Label Warning

- I will discuss the following off-label use in this presentation: Treatment for acute HCV

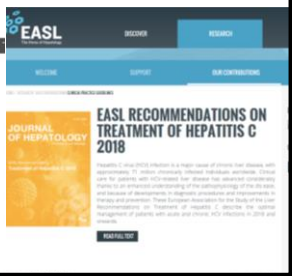
## Learning Objectives

After attending this presentation, learners will be able to:

- Describe diagnostic testing strategies for HCV and when to do testing for HCV resistance
- List treatment options for treatment naïve patients
- Identify the advantages and limitations of newly approved HCV treatment regimens

**IDSA/AASLD**
**www.hcvguidelines.org**


**EASL**
http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/easl-recommendations-on-treatment-of-hepatitis-c-2018




## ARS Question #1: Which of the following patients does the CDC currently recommend should be offered HCV testing?

1. 45 W on hemodialysis
2. 54 midwestern M with normal liver enzymes
3. 33 pregnant W from Egypt
4. 41 M with HIV acquired through sex
5. All of the above
6. All but #2 and #3
7. All but #3

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## Current CDC recommendations for HCV Testing

**Test once (no risk assessment):**
- **Adults born 1945-1965**

**Uncertain**
- Long term sexual partner of HCV+
- STIs or multiple sex partners
- Intranasal drug use
- Tattooing/bodypiercing

**Not recommended**
- Health-care, emergency medical, and public safety workers
- *Pregnant women*
- Household (nonsexual) contacts of HCV-positive persons
- *General population*

**Test based on risk for exposure:**
- Currently injecting drugs
- Ever injected drugs
- Have certain medical conditions, including :
  - received clotting factor pre 1987
  - long-term hemodialysis
  - with persistently abnormal alanine aminotransferase levels (ALT)
  - who have HIV infection
- Were prior recipients of transfusions or organ transplants, including persons who:
  - were notified that they received blood from a donor who later tested positive for HCV infection
  - Pre July 1992

**Test based on a recognized exposure**:
- Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood
- Children born to HCV-positive women

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https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm

## Recommendation for Universal Hepatitis C Screening in Pregnancy

| RECOMMENDED | RATING |
|---|---|
| All pregnant women should be tested for HCV infection (see *Recommendations for Initial HCV Testing and Follow-Up*), ideally at the initiation of prenatal care. | IIb, C |

## Recommendation Regarding HCV Treatment and Pregnancy

| RECOMMENDED | RATING |
|---|---|
| For women of reproductive age with known HCV infection, antiviral therapy is recommended before considering pregnancy, whenever practical and feasible, to reduce the risk of HCV transmission to future offspring. | I, B |

## Not Recommended Regarding HCV Treatment and Pregnancy

| NOT RECOMMENDED | RATING |
|---|---|
| Treatment during pregnancy is not recommended due to the lack of safety and efficacy data. | IIb, C |

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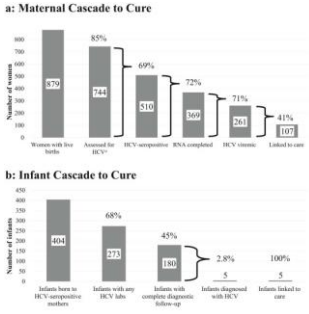


- "HCV prevalence among pregnant women with opioid use is high and infant HCV screening is imperfect. Programmatic changes to improve both mother and infant follow-up may help to bridge identified gaps in the cascade to cure"

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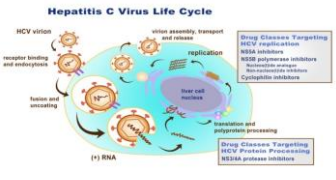
## Strategy for Initial HCV therapy: Direct acting antivirals target life cycle




---**PR**EVIR
**Pr**otease inhibitors
e.g. *telaprevir, boceprevir,* faldaprevir, simeprevir, danoprevir, asunaprevir, paritaprevir, grazoprevir, voxilaprevir, glecaprevir

---BUVIR
Polymerase inhibitors
- Nucleos(t)ide analogs: e.g. tegobuvir, sofosbuvir,
- Non-nucs: e.g. deleobuvir, dasabuvir

---**AS**VIR
NS**5A** inhibitors
e.g. daclatasvir, ledipasvir, ombitasvir, elbasvir, velpatasvir, pibrentasvir

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ARS Question #2: Which of the following represents the BEST strategy for treating HCV?

1. 3 drugs for 8 weeks
2. 2 drugs for 8 weeks
3. 2 drugs for 12 weeks
4. 3 drugs for 12 weeks

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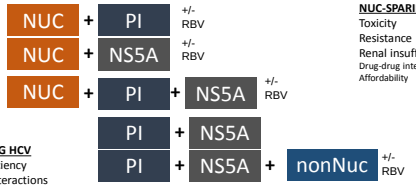
## Currently used combinations of DAA classes




**NUC-SPARING HIV**
Toxicity
Resistance
Renal insufficiency
Drug-drug interactions
Affordability

**NUC-SPARING HCV**
Renal insufficiency
Drug-drug interactions
Duration
Affordability/Access
Toxicity
Resistance

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## Approved Drug Regimens for Initial Treatment

| | PEG RBV SOF | RBV SOF | RBV SMV SOF | LDV SOF | DAC SOF | RBV PTV/r OMV DAS | GZR EBV | VEL SOF | GLE PBV |
|---|---|---|---|---|---|---|---|---|---|
| Interferon | PegIFN | | | | | | | | |
| Ribavirin | ribavirin | ribavirin | +/-ribavirin | | | +/-ribavirin | | | |
| Nucs | sofosbuvir | sofosbuvir | sofosbuvir | sofosbuvir | sofosbuvir | | | sofosbuvir | |
| Protease inhibitors | | | simeprevir | | | Paritaprevir /ritonavir | grazoprevir | velpatasvir | glecaprevir |
| NS5A | | | | ledipasvir | daclatasvir | ombitasvir | elbasvir | | pibrentasvir |
| Non-Nucs | | | | | | dasabuvir | | | |
| G1 | x | x | X | X | X | X | X | X | X |
| G2 | x | X | | | x | | | X | X |
| G3 | X | x | | | X | | | X | X |
| G4 | x | X | x | X | x | X | X | X | X |

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## First-line HCV Therapy: Distinguishing Among Recommended Options

EBR/GZR - QD single tablet
12 wks, GT 1 or 4
Requires RAS testing for GT1a
Contains PI: *do not use* if decompensated
Can be used in stage 4/5 CKD
DDI highlights: glucocorticoids, statins, PDE inhibitors, rifampin

DDIs are drug specific and there are many more to consider than are listed here. Always check! https://www.hep-druginteractions.org/

AASLD/IDSA. HCV guidance. September 2017.

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Slide credit: clinicaloptions.com

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GLE/PIB - QD 3 tablets with food
8 wks no cirrhosis, 12 wks if cirrhosis, GT 1-6
No RAS testing
Contains PI: *do not use* if decompensated
Can be used in stage 4/5 CKD
DDI highlights: statins, rifampin

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8 wks no cirrhosis, 12 wks if cirrhosis, GT 1-6
No RAS testing
Contains PI: *do not use* if decompensated
Can be used in stage 4/5 CKD
DDI highlights: statins, rifampin

LDV/SOF - QD single tablet
8-12 wks, GT 1, 4, 5, or 6
No RAS testing
Safe in decompensation
*Not recommended* for stage 4/5 CKD
DDI highlights: acid-reducing agents, statins, rifampin

DDIs are drug specific and there are many more to consider than are listed here. Always check! https://www.hep-druginteractions.org/

AASLD/IDSA. HCV guidance. September 2017.

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## First-line HCV Therapy: Distinguishing Among Recommended Options

| | |
|---|---|
| EBR/GZR - QD single tablet<br>12 wks, GT 1 or 4<br>Requires RAS testing for GT1a<br>Contains PI: *do not use* if decompensated<br>Can be used in stage 4/5 CKD<br>DDI highlights: glucocorticoids, statins, PDE inhibitors, rifampin | GLE/PIB - QD 3 tablets with food<br>8 wks no cirrhosis, 12 wks if cirrhosis, GT 1-6<br>No RAS testing<br>Contains PI: *do not use* if decompensated<br>Can be used in stage 4/5 CKD<br>DDI highlights: statins, rifampin |
| LDV/SOF - QD single tablet<br>8-12 wks, GT 1, 4, 5, or 6<br>No RAS testing<br>Safe in decompensation<br>*Not recommended* for stage 4/5 CKD<br>DDI highlights: acid-reducing agents, statins, rifampin | SOF/VEL - QD single tablet<br>12 wks, GT 1-6<br>Requires RAS testing for some GT 3<br>Safe in decompensation<br>*Not recommended* for stage 4/5 CKD<br>DDI highlights: acid-reducing agents, rifampin |

DDIs are drug specific and there are many more to consider than are listed here.
Always check! https://www.hep-druginteractions.org/

AASLD/IDSA. HCV guidance. September 2017.

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## Previously Challenging Clinical Scenarios – SVR now >95%

- Black patients
- ESRD
- HIV/HCV
- Post-liver transplant
- G3 + cirrhosis

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## CASE 1 – Initial Treatment and when to do resistance testing

26 y.o. Caucasian Woman with HCV Geno 1b, no cirrhosis , HCV RNA 1.2 mil IU/mL

HCV Hx:

**Diagnosed during last pregnancy**
Risk factor IVD last use 26 mos ago
Treatment naïve
Fibrosure F0

Other med hx includes:

Seizure disorder on keppra

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ARS Question #3: Which of the following regimens would NOT be recommended for this patient with HCV g1b and no cirrhosis?

1. Sofosbuvir/velpatasvir/voxilaprevir x 8 wks
2. Sofosbuvir/velpatasvir x 12 wks
3. Sofosbuvir/ledipasvir x 8 wks
4. Glecaprevir/pibrentasvir x 8 wks

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## Minimum to Know Pre-Treatment

- HCV genotype/subtype
- HCV resistance (sometimes)
- Stage of fibrosis
  - Cirrhosis - yes/no
    - If yes, decompensated? (e.g., ascites, encephalopathy, etc)
      - If yes, **don't use PIs**!
  - Method?
    - Liver biopsy
    - Transient elastography
    - Laboratory biomarkers
    - Imaging
- Prior HCV treatment?
  - Response?
  - DAA used?
- Medications
  - To check for drug interactions
- Comorbidities
  - Renal function
  - HIV status
  - Life expectancy < 1yr non-liver causes?
- Patient preference
- Child-bearing potential of patient/partner
  - Ribavirin is a teratogen

HIV/Hepatitis C helpline
1-866-637-2342

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## G1b Initial Treatment Recommended Regimens

**IDSA/AASLD**

**www.hcvguidelines.org**

| NO CIRRHOSIS: | CIRRHOSIS: |
|---|---|
| Elbasvir/grazoprevir x 12 w | Elbasvir/grazoprevir x 12 w |
| Glecaprevir/pibrentasvir x 8 w | Glecaprevir/pibrentasvir x 12 w |
| Ledipasvir/sofosbuvir x 8* or 12 w | Ledipasvir/sofosbuvir x 12 w |
| Sofosbuvir/velpatasvir x 12 w | Sofosbuvir/velpatasvir x 12 w |

*8 wk not recommended for Black patients or HIV-infected. Only recommended when RNA< 6 million IU/ml

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## CASE 1 – cont

26 y.o. Caucasian Woman with HCV Geno 1b, no cirrhosis (F0) HCV RNA 1.2 mil IU/mL on leviteracetam prescribed 8 weeks of sofosbuvir/ledipasvir.

**ARS Question #4: True or false? Resistance testing should be performed prior to treatment.**

1. True
2. False

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## RAS Testing prior to Treatment

- NS5A RASs are relatively common (10-15%)
- Significance of NS5A RASs may depend on the RAV, the genotype, the regimen used and whether prior NS5A treatment
- In initial treatment, use resistance testing prior to:
  - Treatment with grazoprevir/elbasvir for 1a
  - Treatment with sofosbuvir/velpatasvir for G3 with cirrhosis

**Table: Clinically Significant NS5A Resistance-Associated Variants (RAVs)**

| Wild-type Amino Acid (sensitive) | Position | Variant Amino Acid (reduced EBR activity) |
|---|---|---|
| M | 28 | A/G/T |
| Q | 30 | D/E/H/G/K/L/R |
| L | 31 | F/M/V |
| Y | 93 | C/H/N/S |

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## G1a Initial Treatment Recommended Regimens

**IDSA/AASLD**

**www.hcvguidelines.org**

NO CIRRHOSIS:

- Elbasvir/grazoprevir x 12 w if no hi level NS5A resistance
- Glecaprevir/pibrentasvir x 8 w
- Ledipasvir/sofosbuvir x 8* or 12 w
- Sofosbuvir/velpatasvir x 12 w

CIRRHOSIS:

- Elbasvir/grazoprevir x 12 w if no hi level NS5A resistance
- Glecaprevir/pibrentasvir x 12 w
- Ledipasvir/sofosbuvir x 12 w
- Sofosbuvir/velpatasvir x 12 w

*8 wk not recommended for Black patients or HIV-infected

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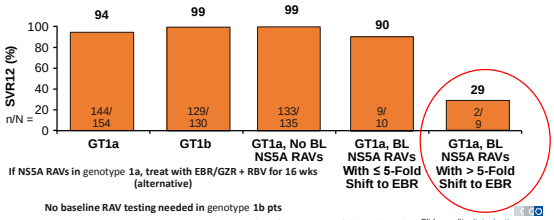
## Impact of Baseline NS5A RAVs:

**SVR12 With 12 Wks of Grazoprevir/Elbasvir for initial treatment**




**If NS5A RAVs in** genotype **1a, treat with EBR/GZR + RBV for 16 wks (alternative)**

**No baseline RAV testing needed in** genotype **1b pts**

Zeuzem S, et al. Ann Intern Med. 2015;163:1-13. Slide credit clinicaloptions.com

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## Team Approach to HCV Treatment
## Pre-treatment, Pre-approval

**My Contribution**

- Work with patient to pick regimen
- Clearly describe in plan ANY indications for treatment
  - E.g. HCV st 2 fibrosis, woman of child bearing potential, cryoglobulins, DM, etc.
- Clearly describe in my plan the indications for this SPECIFIC regimen
  - E.g. G1a, Tx-naïve, cirrhosis – LDV/SOF x 12 wks
  - If unusual choice - cite study or guidance document
- Clearly describe in my plan the reasons other regimens NOT a good option
  - E.g. current darunavir/r use precludes use of PrOD
- Confirm discussed medication interactions and address any specific ones
- Document no barriers to adherence evidenced by HIV control, etc

**Contribution of Hepatitis Nurses +/or Pharmacy**

- Complete specialty pharmacy referral
- Print any relevant lab/imaging documentation
- Fax to specialty pharmacy
  - File and Track progress
- Help draft letters for Appeals
  - File and Track progress
- Stay in communication with patient
- Patient assistance connections when needed
  - Copay programs
  - Charity

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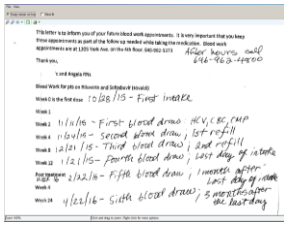
## Team Approach to HCV Treatment
## Pre-treatment, Post-approval

**Meet with Hepatitis Nurses only**

- Drugs usually delivered to our clinic
- Review any new medications
- Education about medications
- Discussion of side effects and management
- Create monitoring plan schedule
- Book appointments for monitoring visits
  - Local Quest lab if cannot make to our clinic
- Review how to take and usually take first dose

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## Initial Treatment Algorithm

Algorithm

- HCV genotype/subtype & resistance
- HIV status
- Cirrhosis - yes/no - duration
  - If yes, decompensated? (e.g., ascites, encephalopathy, etc)
    - If yes, **don't use PIs**!
- Renal function
  - Avoid Sof if CrCl <30
- Medications
  - Address drug interactions
  - Ribavirin is a teratogen
- On treatment/Follow up specifics

Our case patient

- 1b, no need for resistance testing, choose from 4 recommended regimens
- HIV neg
- Cirrhosis – No
  - Could use 8 wk regimen if meet criteria
- CrCl nl
- Medications: PPI qd
  - Elbasvir/grazoprevir – no interaction
  - Glecaprevir/pibrentasvir (limit dose)
- Follow up: h/o IVD, rescreen and ensure adequate supportive services (psych, harm reduction)

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## CASE 2 – What to use in patient with ESRD

45 y.o. African American M with HCV Geno2 and cirrhosis, HCV RNA 221,000 IU/mL

HCV Hx:

Treatment naïve

Cirrhotic based on transient elastography measurement of 17 kpa

No decompensation events

EGD no varices

Sono mildly nodular, no HCC

Other med hx includes:

HTN, high cholesterol

ESRD on hemodialysis

Mild GERD on PPI qD

HBV sAg+ cAb+ sAb-, HBV DNA negative

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## G2 INITIAL TREATMENT RECOMMENDED REGIMENS

**IDSA/AASLD/IAS-USA**

**www.hcvguidelines.org**

NO CIRRHOSIS:

Glecaprevir/pibrentasvir x 8 w

Sofosbuvir/velpatasvir x 12 wks

CIRRHOSIS:

Glecaprevir/pibrentasvir x 12 w

Sofosbuvir/velpatasvir x 12 wks

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## ARS Question #5: Prior to treatment, you recommend which following additional evaluation?

1. Hepatitis B genotype
2. HCV resistance test
3. MRI to evaluate for Hepatocellular carcinoma
4. Transplant center referral

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## ARS Question #6: Your patient is not interested in kidney transplant at this time. Which of the following treatments do you recommend?

1. Elbasvir/grazoprevir x 12 w
2. Glecaprevir/pibrentasvir x 8w
3. Glecaprevir/pibrentasvir x 12w
4. Sofosbuvir/velpatasvir x 12 wks

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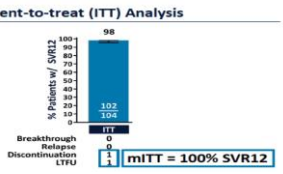
## Glecaprevir/pibrentasvir: Renal Impairment

- GT 1-6 for 12 weeks
- Stage 4 or 5 CKD
  - GFR<30 including HD
  - 82% on HD
- TN or TE (42%) with IFN, P/R or SOF+P/R
- Including compensated cirrhosis (19%)
- GT1a 22%, GT1b 28%, GT2 16%, GT3 11%, GT4 19%, GT5 1, GT6 11




Gane et al. EASL 2017

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**Recommended regimens listed by evidence level and alphabetically for:**

**Patients With CKD Stage[a] 4 or 5 (eGFR <30 mL/min or End-Stage Renal Disease)**

| RECOMMENDED | GENOTYPE | DURATION | RATING |
|---|---|---|---|
| Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) | 1a, 1b, 4 | 12 weeks | I, B |
| Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b] | 1, 2, 3, 4, 5, 6 | 8 to 16 weeks[c] | I, B[c] |

[a] Chronic kidney disease (CKD) stages: 1 = normal (eGFR >90 mL/min); 2 = mild CKD (eGFR 60-89 mL/min); 3 = moderate CKD (eGFR 30-59 ml/min); 4 = severe CKD (eGFR 15-29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min)
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.
[c] Patients in this group should be treated as would patients without CKD. Duration of glecaprevir/pibrentasvir should be based on presence of cirrhosis and prior treatment experience (please refer to appropriate section). As such, strength of rating may be lower for certain subgroups.

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## CASE 2 – cont

45 y.o. African American M with HCV Geno2 and compensated cirrhosis, HCV RNA 221,000 IU/mL, ESRD, prescribed glecaprevir/pibrentasvir x 12 weeks.
Four weeks into treatment, he comes in for labs and complains of some malaise. Exam unchanged with no evidence of ascites or edema.

Labs reveal:
HCV RNA not detected
AST 120 IU/ml (baseline 35)
ALT 155 IU/ml (baseline 33)
Bili 1.9 mg/dl (baseline 1.0)

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## ARS Question #7: What do you do next?

1. Immediately discontinue his HCV treatment and admit to hospital
2. Discontinue HCV treatment and order labs
3. Continue HCV treatment and order labs

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## Some potential explanations:

- Hepatitis B reactivation
- Hepatic decompensation from HCV protease inhibitor
- Another viral infection
- Drug-induced liver injury

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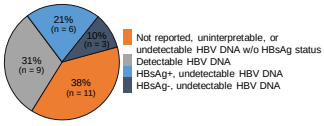
## HBV Reactivation in Pts Receiving HCV DAAs: Postmarketing Cases Reported to FDA

- 29 confirmed cases of HBV reactivation in HCV DAA recipients in ~ 3 yrs (November 2013 to October 2016)
  - Most cases occurred within 4-8 wks of initiation




- Outcome:
  - Transplant (n = 1)
  - Death (n = 2)
  - Hospitalization (n= 3)
  - Other (n = 20)

Bersoff-Matcha SJ, et al. AASLD 2016. Abstract LB-17.

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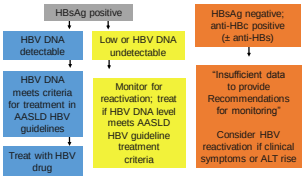
## HBV Testing/Monitoring During HCV DAA Therapy

- Test all pts initiating HCV therapy for HBsAg, anti-HBc, and anti-HBs
  - Vaccinate if no HBV markers; follow flow chart below if HBV markers present




AASLD/IDSA. HCV Guidelines 2016. Graphic adapted from Ira M. Jacobson, MD.

Slide credit: clinicaloptions.com

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## Initial Treatment Algorithm

Algorithm

- HCV genotype/subtype & resistance
- HIV status
- Cirrhosis - yes/no - duration
  - If yes, decompensated? (e.g., ascites, encephalopathy, etc)
    - If yes, **don't use PIs**!
- Renal function
  - Avoid Sof if CrCl <30
- Medications
  - Address drug interactions
  - Ribavirin is a teratogen
- On treatment/Follow up

Our case patient

- 2, no need for resistance testing, start with 2 recommended regimens
- HIV neg
- Cirrhosis – yes
  - No 8 wk regimens
  - Compensated so ok to use PIs
- CrCl <30, no regimens w/ sofosbuvir
- Medications: PPI qd
  - Elbasvir/grazoprevir – no interaction
  - Glecaprevir/pibrentasvir (limit dose)
- Cirrhosis needs monitoring, HBV sAg+ needs monitoring

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## CASE 3 – HIV/HCV coinfection

29 y.o. Hispanic M with HIV, HCV Geno 3, F2 by Fibrosure (and nl liver labs)

HCV Hx:

Acquired 3 yrs ago, only RF unprotected sex with 2 partners

Treatment naïve

F2 by Fibrosure

HIV Hx: Diagnosed 8 yrs ago, CD4 475

HIV RNA not detected on TDF/FTC/EFV

Other PMH:

Recent LGV infection

HBV sAg- cAb+ sAb-, HBV DNA negative

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## ARS Question #8: You check his formulary and his insurance covers GLE/PIB x 8 wks. You need to make an adjustment for which of the following reasons?

1. 8 weeks is not appropriate for patients with HIV
2. He needs TDF switched to TAF
3. GLE/PIB should not be administered with EFV
4. GLE/PIB does not cover Genotype 3 well

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## Treatment Recommendations for Patients With HIV/HCV Coinfection

| RECOMMENDED | RATING |
|---|---|
| HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see *Initial Treatment of HCV Infection* and *Retreatment of Persons in Whom Prior Therapy Has Failed*). | I, B |
| Daily daclatasvir (refer to information above for dose) plus sofosbuvir (400 mg), with or without ribavirin, is a recommended regimen when antiretroviral regimen changes cannot be made to accommodate alternative HCV direct-acting antivirals. Refer to *Initial Treatment of HCV Infection* and *Retreatment of Persons in Whom Prior Therapy Has Failed* sections for treatment duration. | I, B |

## Regimens Not Recommended for Patients With HIV/HCV Coinfection

| NOT RECOMMENDED | RATING |
|---|---|
| Ledipasvir/sofosbuvir for 8 weeks is not recommended, regardless of baseline HCV RNA level. | IIb, C |

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## G3 INITIAL TREAMENT RECOMMENDED REGIMENS

### IDSA/AASLD/IAS-USA

**www.hcvguidelines.org**

NO CIRRHOSIS:

Glecaprevir/pibrentasvir x 8 w

Sofosbuvir/velpatasvir x 12 w

CIRRHOSIS:

Glecaprevir/pibrentasvir x 12 w

Sofosbuvir/velpatasvir x 12 w*

*RAV testing for Y93H and add RBV if present or consider sofosbuvir/velpatasvir/voxilaprevir

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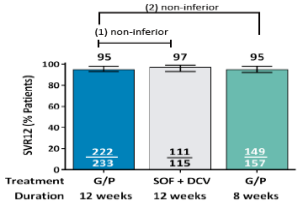
## Glecaprevir/pibrentasvir in GT3 Treatment-naïve without Cirrhosis

- Non-inferiority
  - 12W vs DAC/SOF X12W
  - 12W vs 8W
- Viral Failure 3% G/P
  - 4 in 12W (3 relapse, 1 VBT)
  - 1 in DAC/SOF
  - 6 in 8W (5 relapse, 1 VBT)
- BL Y93H: 5/5 SVR
- BL dual NS3/NS5A
  - 71-86% SVR
- Tx emergent RAS
  - 50% failures with A30K BL
  - A30K+Y93 (69-fold R




**SURVEYOR-II – G3 with Cirrhosis**

**48 patients received G/P +/- RBV x 12 w = 100% SVR**

**Foster et al. EASL 2017**

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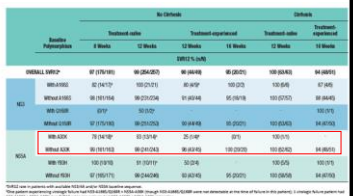
## Glecaprevir/pibrentasvir in GT3 Treatment-naïve without Cirrhosis – A30K effect?

- Non-inferiority
  - 12W vs DAC/SOF X12W
  - 12W vs 8W
- Viral Failure 3% G/P
  - 4 in 12W (3 relapse, 1 VBT)
  - 1 in DAC/SOF
  - 6 in 8W (5 relapse, 1 VBT)
- Tx emergent RAS
  - 50% failures with A30K BL
    - 6% patients overall had a BL A30K

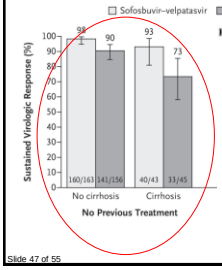


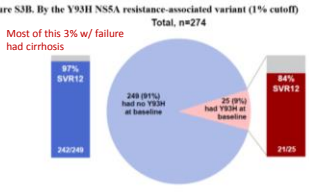
**SURVEYOR-II – G3 with Cirrhosis**
**48 patients received G/P +/- RBV x 12 w = 100% SVR**

Foster et al. EASL 2017 Krishnan et al. EASL 2017



## Sofosbuvir/velpatasvir x 12 wks for G3 (ASTRAL-2)



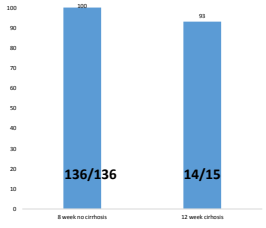




*Foster, NEJM, 2015, hcvguidelines.org*



## Glecaprevir/pibrentasvir: HIV

- GT 1-6
- Primarily an 8 week study
- 12 weeks in 16 patients with cirrhosis
- TN or TE (19%) with IFN, P/R or SOF+P/R
- VBT on treatment – GT3 with cirrhosis




Rockstroh et al. EASL 2017

## Drug Interactions Between DAAs and ARV Drugs—Recommended Regimens

Green indicates coadministration is safe, yellow indicates dose change or additional monitoring is warranted, pink indicates combination should be avoided.

| | Ledipasvir/ Sofosbuvir (LDV/SOF) | Sofosbuvir/ Velpatasvir (SOF/VEL) | Elbasvir/ Grazoprevir (EBR/GRZ) | Glecaprevir/ Pibrentasvir (GLE/PIB) | Sofosbuvir/Velpatasvir/ Voxilaprevir (SOF/VEL/VOX) |
|---|---|---|---|---|---|
| Ritonavir-boosted atazanavir (ATZ) | ▲ LDV ▲ ATZ* | ▲ VEL ▲ ATZ* | ▲ ELB ▲ GRZ ▲ ATZ | ▲ GLE ▲ PIB ▲ ATZ | ▲ VOX ▲ ATZ |
| Ritonavir-boosted darunavir (DRV) | ▲ LDV ◀▶ DRV* | ◀▶ VEL ◀▶ DRV* | ▲ ELB ▲ GRZ ◀▶ DRV | ▲ GLE ◀▶ PIB ▲ DRV | ▲ VOX ▼ DRV |
| Ritonavir-boosted lopinavir (LPV) | No data* | ◀▶ VEL ◀▶ LPV* | ▲ ELB ▲ GRZ ◀▶ LPV | ▲ GLE ▲ PIB ▲ LPV | No data |
| Ritonavir-boosted tipranavir (TPV/r) | No data | No data | No data | No data | No data |
| Efavirenz (EFV) | ▼ LDV ▼ EFV* | ▼ VEL ▼ EFV | ▼ ELB ▼ GRZ ▼ EFV | No data | No data |
| Rilpivirine (RPV) | ◀▶ LDV ◀▶ RPV | ◀▶ VEL ◀▶ RPV | ◀▶ ELB ◀▶ GRZ ◀▶ RPV | ◀▶ GLE ◀▶ PIB ▲ RPV | ◀▶ VOX ▼ RPV |
| Etravirine (ETV) | No data | No data | No data | No data | No data |
| Raltegravir (RAL) | ◀▶ LDV ◀▶ RAL | ◀▶ VEL ◀▶ RAL | ◀▶ ELB ◀▶ GRZ ▲ RAL | ◀▶ GLE ◀▶ PIB ▲ RAL | No data |
| Cobicistat-boosted elvitegravir (COBI) | ▲ LDV ▲ COBI* | ▲ VEL ▲ COBI* | ▲ ELB ▲ GRZ ▲ COBI | ▲ GLE ▲ PIB ▲ COBI | ▲ VOX ▲ COBI* |
| Dolutegravir (DTG) | ◀▶ LDV ◀▶ DTG | ◀▶ VEL ◀▶ DTG | ◀▶ ELB ◀▶ GRZ ▲ DTG | ▼ GLE ▼ PIB ▲ DTG | No data |
| Tenofovir Alafenamide (TAF) / Emtricitabine (FTC) /Bictegravir (BIC) | ▼ LDV ◀▶ BIC | No data | No data | No data | ◀▶ VOX ▲ BIC |
| Maraviroc (MVC) | No data | No data | No data | No data | No data |
| Tenofovir (TFV) disoproxil fumarate | ◀▶ LDV ▲ TFV* | ◀▶ VEL ▲ TFV* | ◀▶ ELB ◀▶ GRZ ▲ TFV | ▲ TFV | ▲ TFV* |
| Tenofovir (TFV) alafenamide | ◀▶ LDV ▲ TFV* | ◀▶ VEL ▲ TFV* | No data | ◀▶ TFV | ▲ TFV* |

* Caution only with tenofovir disoproxil fumarate. ^ Increase in tenofovir depends on which additional concomitant antiretroviral agents are administered. ‡ Avoid tenofovir disoproxil fumarate in patients with an eGFR <60 mL/min. tenofovir concentrations may exceed those with established renal safety data in individuals on ritonavir- or cobicistat-containing regimens. ° Studied as part of fixed-dose combinations with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir plus TAF, emtricitabine, elvitegravir, and cobicistat.

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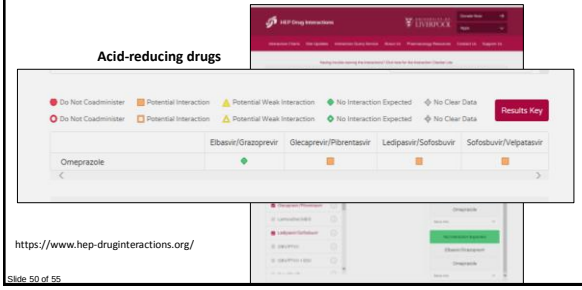
## Drug-Drug Interactions with DAAS

**Acid-reducing drugs**




https://www.hep-druginteractions.org/

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## Guidelines Recommendation about use of LDV or VEL with TDF

SOF/LDV + TDF

CrCl < 60 mL/min: AVOID

CrCl > 60: MONITOR

SOF/VEL + TDF

CrCl < 60 mL/min: AVOID

CrCl > 60: MONITOR

SOF/LDV + TDF + cobi- or ritonavir-boosted PI

Any CrCl: AVOID if possible, Consider TAF

SOF/VEL + TDF + cobi- or ritonavir-boosted PI

CrCl < 60 mL/min: AVOID

CrCl > 60: MONITOR or consider TAF

- **For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended.**
  Rating: Class IIa, Level C

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## CASE 3 – HIV/HCV coinfection (Cont)

His ARVS are changed to TAF/FTC/BIC and he is tolerating well. He receives 8 weeks of GLE/PIB and achieves SVR12.

**ARS Question #9: True or False: His risk of HCV reinfection is extremely low. No further follow up testing is recommended.**

1. True
2. False

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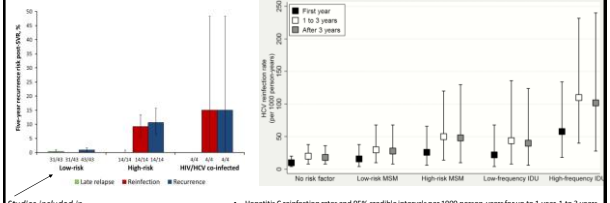
## Re-infection Rates After Treatment by Risk Group




*Studies included in meta-analysis*

- Hepatitis C reinfection rates and 95% credible intervals per 1000 person-years for up to 1 year, 1 to 3 years, and more than 3 years after a sustained virologic response (Canadian Co-infection Cohort, n = 257). Reference patients are those with no risk factors. Abbreviations: HCV, hepatitis C virus; IDU, injection drug use; MSM, men who have sex with men.

Clin Infect Dis. 2016;62(6):683–94

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## Initial Treatment Algorithm

Algorithm

- HCV genotype/subtype & resistance
- HIV status
- Cirrhosis - yes/no - duration
  - If yes, decompensated? (e.g., ascites, encephalopathy, etc)
    - If yes, **don't use PIs**!
- Renal function
  - Avoid Sof if CrCl <30
- Medications
  - Address drug interactions
  - Ribavirin is a teratogen
- On treatment/Follow up

Our case patient

- 3, resistance testing recommended if cirrhosis and epclusa
- HIV – check drug drug interactions (efavirenz)
- Cirrhosis – no
  - 8 wk regimens
- CrCl nl, SOF ok
- Medications: efavirenz – not recommended with SOF/VEL or GLE/PIB
- need to monitor for HCV reinfection

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# Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!

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