What a Difference a Year Makes: Advances in Hepatitis C Treatment for HIV/HCV Co-infected Patients

Kara Chew, MD
Assistant Clinical Professor
David Geffen School of Medicine at UCLA

Disclosures

• Disclosures: Research support awarded to the institution from Gilead and Merck

Outline

• Whom to screen and treat for HCV
• How to choose between the different HCV treatment regimens for genotype 1 infection
• Drug interactions between HCV direct-acting antiviral agents (DAAs) and antiretroviral therapy
• Treatment of HCV genotype 2 and 3 infection
• Treatment in renal failure
• FDA warnings
HCV screening and treatment in HIV-infected patients

- All HIV-infected patients should be screened for HCV.
- Annual HCV screening in high-risk patients and when suspected clinically.
- Antiretroviral therapy (ART) should be initiated in all HIV/HCV co-infected patients, regardless of CD4 cell count.
- If CD4 > 500 cells/mm³ and HIV treatment naive, can consider deferring ART until completion of HCV treatment (pill burden, drug interactions, toxicities).
- If CD4 < 200 cells/mm³, initiate ART and treat HCV when stable on HIV treatment.
- HCV treatment recommended for all patients with HCV, except if life expectancy is short and without viable intervention.


Case: JP

48 y.o. African-American man with HIV/HCV coinfection. He has a prior history of heavy alcohol use but has abstained for the past 5 years. He has been virologically suppressed on FDC efavirenz/tenofovir disoproxil fumarate (TDF)/emtricitabine for 8 years and has not been interested in switching off this ART regimen. HCV treatment naive.

PMH: hypertension, dyslipidemia, "gastritis"

Medications: EFV/TDF/FTC, amlodipine 5 mg daily, HCTZ 25 mg daily, atorvastatin 20 mg daily, omeprazole 20 mg daily, multivitamin daily

Case: JP

Exam: BP 128/76, HR 70, BMI 28

No jaundice, normal abdominal exam, no spider nevi or palmar erythema, no edema

<table>
<thead>
<tr>
<th>Lab</th>
<th>Result</th>
<th>Lab</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA</td>
<td>&lt;20 copies/mL</td>
<td>Creatine</td>
<td>0.8 mg/dL (0.8-1.5)</td>
</tr>
<tr>
<td>CD4 absolute</td>
<td>727 cells/µL</td>
<td>Neutrophils</td>
<td>47 %</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>6,350,000 IU/mL</td>
<td>ANC</td>
<td>4700/µL</td>
</tr>
<tr>
<td>HCV genotype</td>
<td>1a</td>
<td>Bilirubin</td>
<td>0.7 mg/dL</td>
</tr>
<tr>
<td>WBC</td>
<td>6.5 x 10³/µL</td>
<td>Aspartate aminotransferase</td>
<td>37 U/L</td>
</tr>
<tr>
<td>Hemoglobin/Hematocrit</td>
<td>14.1 g/dL /41.7%</td>
<td>ALAT</td>
<td>220 U/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>220,000</td>
<td>ALAK</td>
<td>8.5 U/L</td>
</tr>
<tr>
<td>NR</td>
<td>1.1</td>
<td>Fibrousme</td>
<td>71</td>
</tr>
</tbody>
</table>
48 y.o. African-American man with well-controlled HIV on EFV/TDF/FTC, HCV genotype 1a, non-cirrhotic, HCV treatment naive, amlodipine 5 mg daily, HCTZ 25 mg daily, atorvastatin 20 mg daily, omeprazole 20 mg daily, multivitamin daily. **WHAT DO YOU SELECT FOR HCV TREATMENT?**

A) Ledipasvir/sofosbuvir 90mg/400mg once daily x 12 wks  
B) Elbasvir/grazoprevir 50mg/100mg once daily x 12 wks  
C) Paritaprevir/ritonavir/ombitasvir (150/100/25mg) once daily + dasabuvir 250mg BID + weight-based RBV x 12 wks  
D) Simeprevir 150mg plus sofosbuvir 400mg once daily x 12 wks  
E) Daclatasvir 90mg plus sofosbuvir 400mg once daily x 12 wks  
F) Sofosbuvir/velpatasvir 400mg/100mg once daily x 12 wks  
G) I'm not sure – that's why I'm here

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**Which of his medications may interact with HCV DAA regimens?**

A) Atorvastatin  
B) HCTZ  
C) Efavirenz  
D) Amlodipine  
E) Omeprazole  
F) All of the above  
G) A, C, D, E

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**Key considerations when choosing between HCV treatment regimens**

- HCV genotype and subtype (1a vs 1b)
- Drug interactions between ART and HCV DAAs
- Drug interactions between HCV DAAs and drugs for comorbidities  
  - E.g. acid-reducing agents, statins, anticonvulsants, dihydropyridines, rifampin, digoxin  
- Cirrhosis status, compensated or decompensated (Child Pugh Class)
- Comorbidities:  
  - Cardiac disease (anemia with RBV, drug interactions with cardiac meds)  
  - Renal insufficiency (limited data for most DAAs with advanced kidney disease/ESRD, increased tenofovir levels with coadministration of ledipasvir and velpatasvir with TDF)
Drug-Drug Interactions: ART and HCV DAAs

<table>
<thead>
<tr>
<th>HCV regimen</th>
<th>Allowed ART</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ledipasvir/sofosbuvir (LDV/SOF)</td>
<td>Most ART allowed</td>
<td>LDV increases tenofovir levels – avoid coadmin with TDF if CrCl &lt;60 mL/min and avoid LDV + TDF with ritonavir- or cobicistat-boosted ART. TAF may be OK.</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir</td>
<td>Raltegravir, dolutegravir, rilpivirine, tenofovir, abacavir, emtricitabine,</td>
<td>NO HIV-1 protease inhibitors or efaviren</td>
</tr>
<tr>
<td></td>
<td>enfuvirtide, lamivudine</td>
<td></td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/ ombitasvir + dasabuvir</td>
<td>Raltegravir, dolutegravir, rilpivirine, tenofovir, enfuvirtide</td>
<td>NO efaviren</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir (SOF/VEL)</td>
<td>Most ART allowed</td>
<td>VEL increases tenofovir levels – avoid coadmin with TDF if CrCl &lt;60 mL/min and avoid VEL + TDF with ritonavir- or cobicistat-boosted ART. TAF may be OK.</td>
</tr>
</tbody>
</table>

**Renal safety of SOF/LDV administered with boosted TDF**

- 159 HIV/HCV, real-world cohort
- SOF/LDV given with ritonavir-boosted HIV PI or elvitegravir/cobicistat/FTC/TDF
- No significant worsening of renal function in this cohort with baseline normal GFR

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Baseline eGFR (mL/min)</th>
<th>Enrolled</th>
<th>Enrolled eGFR (mL/min)</th>
<th>Enrolled eGFR (mL/min)</th>
<th>Enrolled eGFR (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70+</td>
<td>50+12</td>
<td>9+1</td>
<td>50+13</td>
<td>9+1</td>
<td>50+13</td>
</tr>
<tr>
<td>&lt;70+</td>
<td>50+11</td>
<td>9+0</td>
<td>50+17</td>
<td>3+2</td>
<td>50+17</td>
</tr>
</tbody>
</table>

Rare discontinuations due to renal adverse event

Vivanco-Gallo et al, CROI 2016, Abstract 452

**Acid-reducing agents may reduce efficacy of LDV/SOF and SOF/VEL**

- Ledipasvir (and velpatasvir) solubility decreases with increasing pH
- Current FDA label for SOF/LDV allows max omeprazole dose 20 mg daily given simultaneously under fasted conditions
- PPIs not recommended with SOF/VEL

TRIO Study (Tapper et al, Hepatology 2016): BID PPI with lower SVR12, cirrhosis on BID PPI: OR 0.11 for SVR12
You stop his PPI as there was not a clear indication and submit a request for SOF/LDV x 12 weeks.

Scenario 1: They approve the regimen but for only 8 weeks. WHAT NEXT?

A) Treat for 8 weeks
B) Appeal for 12 weeks

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**Ledipasvir/Sofosbuvir in HCV/HIV (ION-4)**

- Open-label, phase 3 12 week treatment
- Treatment naive and experienced GT1 or 4
  - 115 (34%) Black
  - 67 (20%) cirrhotic
  - 8 GT4
- Median CD4 628
- ART:
  - 160 (48%)
  - 29 (9%) RPV/TDF/FTC
  - 146 (44%) RL+TDF/FTC
- Naggie et al, NEJM 2015;378:705-13, Figure from University of Washington Hepatitis Web Study

*• 13 non-SVR, 10 with relapse – all black, 8/10 on efavirenz
--No differences in PK analysis*

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**Shortening therapy for HIV/HCV coinfected patients**

- HCV monoinfection trial ION-3, treatment-naïve, noncirrhotic participants randomized to 8 vs 12 weeks SOF/LDV: higher relapse rates with 8 weeks
  - Post-hoc analysis with no difference (8 vs 12 weeks) in relapse in participants with baseline HCV VL <6,000,000
- Limited data on 8 wk duration in HCV/HIV
- Current AASLD/IDSA HCV guidelines: Shortening therapy is NOT recommended for HIV-infected patients, African-American patients, those with known IL28B CT or TT polymorphism
Scenario 2: Same patient, but he switches ART to DTG/abacavir/lamivudine and is suppressed. You submit the request for SOF/LDV and it is denied. His insurance plan states grazoprevir/elbasvir is preferred. What do you do next?

A) Treat for 12 weeks
B) Treat for 16 weeks with ribavirin
C) Order additional testing

Grazoprevir/elbasvir in HCV/HIV Co-infection (C-EDGE CO-INFECTION)

Daclatasvir + Sofosbuvir in HCV/HIV Co-infection (ALLY-2)
Sofosbuvir/velpatasvir in HCV/HIV: ASTRAL-5

Results: SVR12 by Genotype

**ASTRAL-5 HCV/HIV Coinfection Study**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Genotype</th>
<th>N</th>
<th>Male</th>
<th>Black</th>
<th>Cirrhotic</th>
<th>GT1</th>
<th>ART: DRV, LPV, ATV, RPV, RAL, EVG + TDF/FTC or ABC/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td></td>
<td>106</td>
<td>86%</td>
<td>45%</td>
<td>77%</td>
<td>74%</td>
<td>High SVR with cirrhosis and prior treatment experience</td>
</tr>
</tbody>
</table>

Wyles et al., EASL 2016, Barcelona April 14-17

**Recommended Regimens – HCV Genotype 1a**

<table>
<thead>
<tr>
<th>Treatment naïve and PEG-IFN/RBV experienced non-cirrhotic</th>
<th>Treatment naïve compensated cirrhotic</th>
<th>PEG-IFN/RBV experienced compensated cirrhotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir + simeprevir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir + WBR x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
</tbody>
</table>

WBR = weight-based ribavirin; RBV = ribavirin; Strength of recommendation provided by Class (I, IIa/b, III) and Level (A, B, C).

**Recommended Regimens – HCV Genotype 1b**

<table>
<thead>
<tr>
<th>Treatment naïve and PEG-IFN/RBV experienced non-cirrhotic</th>
<th>Treatment naïve compensated cirrhotic</th>
<th>PEG-IFN/RBV experienced compensated cirrhotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir x 12 weeks (IA) – no resistance testing needed</td>
<td>Elbasvir/grazoprevir x 12 weeks (IA) – no resistance testing needed</td>
<td>Elbasvir/grazoprevir x 12 weeks (IA) – no resistance testing needed</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir + simeprevir x 12 weeks (IA)</td>
<td>Ledipasvir/sofosbuvir x 24 weeks (IA)</td>
<td>Ledipasvir/sofosbuvir + WBR x 12 weeks (IA)</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 weeks (IA)</td>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 weeks (IA)”</td>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 weeks (IA)”</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
</tr>
</tbody>
</table>

WBR = weight-based ribavirin; RBV = ribavirin; Strength of recommendation provided by Class (I, IIa/b, III) and Level (A, B, C).

• FOR RECOMMENDED REGIMENS FOR DAA-EXPERIENCED, SEE AASLD/IDSA HCV GUIDELINES
### Side effects

- Few discontinuations in trials due to adverse effects
- Headache, fatigue, nausea, diarrhea
- Anemia and rash with ribavirin
- Few with mild bilirubin elevations
- Few with ALT elevations (PrOD, grazoprevir/elbasvir)

### Case: AC

- 52 y.o. woman with well-controlled HIV on elvitegravir/cobicistat/TDF/FTC, genotype 3 HCV infection, and compensated cirrhosis. She is HCV treatment naïve.
- PMH: HTN, h/o disseminated MAC, PCP
- Meds: EVG/C/TDF/FTC, lisinopril, albuterol
- Current CD4 799, hemoglobin 13.4, CrCl 58, AST 78, ALT 90, HLA-B*5701 positive, HCV RNA 14,500,000 IU/mL
- Abdominal US shows cirrhosis, no splenomegaly, no mass or other findings

52 y.o. woman with HIV/HCV, genotype 3, HCV treatment naïve, with compensated cirrhosis on EVG/c/TDF/FTC, CrCl 58, HLA-B*5701 positive. What is your next step?

A) Start sofosbuvir/velpatasvir (SOF/VEL) x 12 wks
B) Switch her ART and then start SOF/VEL x 12 wks
C) Start SOF + daclatasvir (DCV) + RBV x 24 weeks
D) Order NS5A resistance testing, switch her ART, and then start SOF/VEL +/- RBV
Sofosbuvir/velpatasvir for HCV genotype 1-6

<table>
<thead>
<tr>
<th>GENOTYPE</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>98% (206/210)</td>
</tr>
<tr>
<td>1b</td>
<td>99% (117/118)</td>
</tr>
<tr>
<td>2</td>
<td>100% (104/104) / 99% (133/134)</td>
</tr>
<tr>
<td>3</td>
<td>95% (264/277) *NS5A RAVs impact SVR</td>
</tr>
<tr>
<td>4</td>
<td>100% (116/116)</td>
</tr>
<tr>
<td>5</td>
<td>97% (34/35)</td>
</tr>
<tr>
<td>6</td>
<td>100% (41/41)</td>
</tr>
</tbody>
</table>

ASTRAL-1, -2, and -3 trials, Feld, NEJM 2015; Foster, NEJM 2015

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### Recommended Regimens

### HCV Genotype 3

<table>
<thead>
<tr>
<th>Treatment naive non-cirrhotic</th>
<th>Treatment naive compensated cirrhotic</th>
<th>PEG-IFN/RBV treatment experienced non-cirrhotic</th>
<th>PEG-IFN/RBV treatment experienced compensated cirrhotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir + sofosbuvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA) - add RBV if RAV present (Y93H)</td>
<td>Daclatasvir + sofosbuvir x 12 weeks (IA) - add RBV if RAV present (Y93H)</td>
<td>Sofosbuvir/velpatasvir + WBR x 12 weeks (IB)</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Daclatasvir + sofosbuvir x 24 weeks +/- WBR (IIaB) - include RBV if +Y93H</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA) - add RBV if RAV present (Y93H)</td>
<td>Daclatasvir + sofosbuvir x 24 weeks + WBR (IIaB)</td>
</tr>
</tbody>
</table>

WBR = weight-based ribavirin, RBV = ribavirin; Strength of recommendation provided by Class (I, IIa/b, III) and Level (A, B, C). PEG-IFN= pegylated interferon

### HCV Genotype 2

<table>
<thead>
<tr>
<th>Treatment naive non-cirrhotic or compensated cirrhotic</th>
<th>PEG-IFN/RBV treatment experienced non-cirrhotic or compensated cirrhotic</th>
<th>Sofosbuvir/RBV experienced non-cirrhotic or cirrhotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Sofosbuvir/velpatasvir x 12 weeks (IA)</td>
<td>Daclatasvir + sofosbuvir +/- WBR x 24 weeks if PEG-IFN and/or RBV ineligible (IIaC)</td>
</tr>
</tbody>
</table>

WBR = weight-based ribavirin, RBV = ribavirin; Strength of recommendation provided by Class (I, IIa/b, III) and Level (A, B, C). PEG-IFN= pegylated interferon
### Treatment in renal impairment

<table>
<thead>
<tr>
<th>Degree of renal impairment</th>
<th>Genotype</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl 30 – 80 mL/min</td>
<td>All genotypes</td>
<td>No dose adjustment needed for Daclatasvir, Ledipasvir/sofosbuvir, Sofosbuvir/velpatasvir, Paritaprevir/ritonavir/ombitasvir, dasabuvir, Sofosbuvir, Sofosbuvir/velpatasvir</td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min including HD</td>
<td>GT 1a or 4</td>
<td>Usual dose Elbasvir (50 mg)/grazoprevir (100 mg) x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>GT 1b</td>
<td>Usual dose Elbasvir/grazoprevir x 12 weeks, Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>GT 2, 3, 5, 6</td>
<td>PEG-IFN + dose-adjusted RBV (200 mg daily)</td>
</tr>
</tbody>
</table>

*High urgency to treat, no immediate option for kidney transplantation*  
ASLD/IDSA HCV Guidance

### FDA Warnings

- Sofosbuvir + amiodarone + another HCV DAA → serious symptomatic bradycardia  
  - Fatal cardiac arrest reported  
  - Bradycardia occurs within hours to days, to up to 2 weeks  
  - Beta blockers or underlying cardiac disease and/or advanced liver disease may increase risk

- Serious liver injury and hepatic decompensation with moderate or severe hepatic impairment with the following regimens:  
  - Paritaprevir/ritonavir/ombitasvir + dasabuvir – contraindicated in Child-Turcotte-Pugh (CTP) B or C disease  
  - Grazoprevir/elbasvir - contraindicated in CTP B and C  
  - Simeprevir combination therapy - not recommended

### FDA Warning: HBV reactivation on HCV treatment (October 4, 2016)

- Reports of HBV reactivation in HBV/HCV co-infected patients during or after HCV treatment with IFN-free DAA regimens  
- Potentially fulminant and fatal  
- Reported in patients both HBsAg positive and with resolved infection (HBsAg negative, anti-HBc positive)  
- Screen for HBV coinfection with HBsAg, anti-HBs, and anti-HBc (all with HIV already should be)  
  - If HBsAg or anti-HBc positive, check HBV DNA  
- Monitor for reactivation on and post treatment

ASLD/IDSA HCV Guidance, www.hcvguidelines.org
### Child-Turcotte-Pugh Score:

**Cirrhosis staging**

<table>
<thead>
<tr>
<th>Score</th>
<th>Bilirubin (mg/dL)</th>
<th>Albumin (g/dL)</th>
<th>PT (INR)</th>
<th>Hepatic Encephalopathy</th>
<th>Ascites (grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;2</td>
<td>&gt;3.5</td>
<td>&lt;1.7</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>2–3</td>
<td>2.8–3.5</td>
<td>1.8–2.3</td>
<td>1–2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>&gt;3</td>
<td>&lt;2.8</td>
<td>&gt;2.3</td>
<td>3–4</td>
<td>Severe</td>
</tr>
</tbody>
</table>

**Child Class**
- **A**: 5–6
- **B**: 7–9
- **C**: >9

Predicts survival (including mortality with surgery) and risk of complications (1-year survival 100% → 80% → 45%)

Pugh et al, Brit J Surg 1973

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### Cirrhotics

- If decompensated (Child Pugh B or C), refer to Hepatology
- EGD for variceal screening
- HCC screening (lifelong)
- Regimens to avoid if CPT B or C: any HCV protease inhibitors
  - Paritaprevir/ritonavir/ombitasvir +/- dasabuvir
  - Grazoprevir/elbasvir
  - Simeprevir

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### Treatment regimen may differ based on cirrhosis status, HCV subtype, prior treatment, baseline resistance

**Depending on the regimen and genotype:**
- Cirrhotics may need to be treated for longer
- Treatment duration may need to be extended and RBV added for cirrhotics and prior treatment failures
- Baseline resistance-associated variants (RAVs) have the greatest impact on genotype 1a and 3 treatment response
- Genotype 1a is harder to treat than 1b - ribavirin may need to be added or resistance testing done with implications for treatment extension
Monitoring on treatment

- Monitor for/counsel on adherence, adverse events, and potential new drug-drug interactions by clinic or telephone visits
- CBC, creatinine/GFR, LFTs, and HCV RNA at week 4
  - ≥10-fold ALT increase → d/c treatment
  - <10-fold ALT increase + symptoms/signs of decompensation → d/c treatment
  - <10-fold ALT increase + asymptomatic → repeat LFTs at weeks 6 and 8
  - If HCV RNA detectable at week 4, repeat quantitative HCV RNA at week 6
    * If HCV viral load increases >10-fold (≥1 log10 IU/mL) on repeat testing → d/c treatment
- More frequent CBC monitoring if receiving RBV

Determining treatment response and post-treatment follow-up

- Quantitative HCV RNA at week 4 on treatment and 12 weeks after treatment completion (SVR12 determination)
- Remind patients that treatment cure does not = HCV immunity
- High rates of reinfection in HIV/HCV co-infected persons
  - HIV+ MSM without IDU, 2-year cumulative reinfection rates 25-33%
  - Continue to review risk factors
- Ongoing cirrhosis/chronic liver disease management

Paritaprevir/ritonavir/ombitasvir +/- dasabuvir and CTP A cirrhosis – LFTs at weeks 2 and 4 – if decompensation develops, d/c HCV treatment

Renal monitoring with ledipasvir + TDF, closer if TDF + ritonavir-boosted HIV protease inhibitor
  - Serum creatinine, electrolytes including phosphorus, urinary protein and glucose

Grazoprevir/elbasvir: LFTs at week 8 (and 12 if 16 week course) – late ALT elevations noted
Resistance emerges with treatment failure

<table>
<thead>
<tr>
<th>Patient</th>
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French cohort, DCV/SOF in n=177
44% cirrhotic, 62% treatment-experienced

Fourati et al, CROI 2016, Abstract 577

No longer a gap in HCV treatment responses between HCV/HIV and HCV

- Treatment responses similar between HCV/HIV and HIV
- Similar safety profile between HCV/HIV and HIV
- Recommended regimens are the same for HCV/HIV and HCV
- Real-world data thus far demonstrate similar high effectiveness as seen in clinical trials

Next-generation, pan-genotypic regimens on the horizon

- Sofosbuvir/velpatasvir/GS-5897
- ABT-493/ABT-530
- MK-3682/grazoprevir/MK-8408
- Genotypes 1-6
- Fixed-dose combination single tablet daily
- No need for ribavirin
- Higher barrier to resistance
- Activity against common RAVs
- Improved efficacy in cirrhotic patients
Take Home Points

• HCV treatment should be considered in all HIV co-infected
• Selection of a treatment regimen is influenced by genotype/subtype, cirrhosis status, prior treatment experience, drug interactions, comorbid disease, payer
• Resistance variants impact treatment response in select scenarios (genotypes 1a and 3 and cirrhosis)
• Resistant variants are selected with treatment failure
• Assess risk for and monitor for HBV reactivation
• CHECK DRUG-DRUG INTERACTIONS
• VISIT THE AASLD/IDSA HCV GUIDELINES FREQUENTLY

Suggested Resources

• University of Liverpool hepatitis drug interactions database: www.hep-druginteractions.org
• AASLD Practice Guidelines for management of cirrhosis
  – Management of Hepatocellular Carcinoma (HCC screening recommendations)
  – Prevention and Management of Gastroesophageal Varices and Variceal Hemorrhage in Cirrhosis
  – www.aasld.org/publications/practice-guidelines-0

Thank you for your attention!