Real World Management of HCV in HIV: Approach to Initial Therapy with focus on new DAAs

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Financial Relationships With Commercial Entities

- Dr Marks was awarded research grants, paid to her institution, from Bristol-Myers Squibb, Gilead Sciences, Inc, and Merck.
Learning Objectives

After attending this presentation, learners will be better able to:

- Describe regimens recommended for initial treatment of HCV infection in HIV-infected persons
- Recognize when to do testing for HCV resistance
- Identify the advantages and limitations of newly approved HCV treatment regimens
Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a Guidance section below, or use the search box to begin.

Contents and Introduction - Select a Page

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EASL RECOMMENDATIONS ON TREATMENT OF HEPATITIS C 2016

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. The long-term impact of HCV infection is highly variable, ranging from minimal histological changes to extensive fibrosis and cirrhosis with or without hepatocellular carcinoma (HCC). The number of chronically infected persons worldwide is estimated to be about 180 million, but most are unaware of their infection. Clinical care for patients with HCV-related liver disease has advanced considerably during the last two decades, thanks to an enhanced understanding of the pathophysiology of the disease, and because of developments in diagnostic procedures and improvements in therapy and prevention.

Download to read more.
Newer strategy for HCV therapy: Direct acting antivirals target life cycle

---PREVIR
Protease 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

---ASVIR
NS5A inhibitors
e.g. daclatasvir, ledipasvir, ombitasvir, elbasvir, velpatasvir, pibrentasvir
Currently used combinations of DAA classes

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

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

NUC + PI + +/- RBV
NUC + NS5A
NUC + PI + PI + NS5A + nonNuc + +/- RBV
# Approved Drug Regimens for Initial Treatment

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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
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 commercial lab if cannot make to our clinic
- Review how to take and usually take first dose
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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https://api.cvent.com/polling/v1/api/polls/sp9h0bw5

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
CASE 1 – Treatment duration: when to use 8 v. 12 wks

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 Levetiracetam (Keppra)
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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https:// api.cvent.com/polling/v1/api/polls/sp-p1qeq

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
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
G1b Initial Treatment Recommended Regimens

IDSA/AASLD
www.hcvguidelines.org

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NO CIRRHOSIS:

- Elbasvir/grazoprevir x 12 w
- Glecaprevir/pibrentasvir x 8 w
- Ledipasvir/sofosbuvir x 8* or 12 w
- Sofosbuvir/velpatasvir x 12 w
- Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 w
- Simeprevir + sofosbuvir 12 w
- Daclatasvir + sofosbuvir x 12 w

CIRRHOSIS:

- Elbasvir/grazoprevir x 12 w
- Glecaprevir/pibrentasvir x 12 w
- Ledipasvir/sofosbuvir x 12 w
- Sofosbuvir/velpatasvir x 12 w
- Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12 w*

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

(BOLDED are regimens approved since last year!)
G1a Initial Treatment Recommended Regimens

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

Paritaprevir/ritonavir/ombitasvir + dasabuvir x 12w

Simeprevir + sofosbuvir 12w

Daclatasvir + sofosbuvir x 12w

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

(BOLDED are regimens approved since last year!)
**Pangenotypic Glecaprevir/pibrentasvir**

**DAA combo naive (TN, PEG/RBV, SOF) & special pops**

- **ENDURANCE (Phase 3)**
  - GT 1 no cirrhosis (8 vs 12W)
  - GT 2 no cirrhosis (12W)
  - GT 3 no cirrhosis (8 and 12W)
  - GT 4-6 (12W)

- **EXPEDITION (Phase 3)**
  - GT 1, 2, 4-6 cirrhosis
  - GT 1-6 HIV
  - GT 1-6 Renal impairment

- **SURVEYOR (Phase 2)**
  - GT 2, 4-6 no cirrhosis 8 weeks
  - GT 3 cirrhosis/TE 12 vs 16 W

- Co-formulated – 3 pills once daily
- Pangengotypic
- Next generation
  - Active vs NS3 RAS at 80, 155, 168 and NS5A RAS at 28, Q30, 31, 93
  - A30K associated with failure in GT3 infection
- Negligible renal excretion
- Contains a protease inhibitor
- Has interaction with acid suppressing meds

G/P Slides courtesy of S. Naggie
Glecaprevir/pibrentasvir: No Cirrhosis

- 8 (N=828) vs 12 (N=1076) weeks
- TN and TE
  - PEG, RBV, SOF
  - No DAA otherwise
- Relapse <1%
- Tx emergent RAS

Puoti et al. EASL 2017
Glecaprevir/pibrentasvir: Cirrhosis

- 12 weeks in N=146
- *Compensated* cirrhosis
- TN or TE (25%) with IFN, P/R or SOF+P/R
- GT1a 33%, GT1b 27%, GT2 23%, GT4 11%, GT5 1%, GT6 5%
- 1 relapse- GT1a

Forns et al. EASL 2017
Sofosbuvir/velpatasvir x 12 wks in HIV/HCV G1-6, Naïve + Rx-exp

ASTRAL-5 HIV/HCV Coinfection Study

Results: SVR4 and SVR12

N=106
29% Rx-exp
18% cirrhosis
12% NS5a RAVs

Of 2 relapses:
1 rx-exp, 0 cirrhosis,
baseline RAVS

Renal fxn looked unchanged in pts or boosted TDF

SVR4

100%

95

106

101

SVR12

95%

95

104*

2 relapse
2 LTFU
1 withdraw consent

Results: SVR12 by Genotype

ASTRAL-5 HIV/HCV Coinfection Study

Genotype
Total 1a 1b 2 3 4

SVR12 (%)

95 95 92 100 92 100

LTFU, lost to follow-up. Error bars represent 95% confidence intervals.


*2 patients pending SVR12 visit, both achieved SVR4
POLARIS-2: 8-Wk SOF/VEL/Voxilaprevir vs. 12-Wk SOF/VEL Not Non-inferior for DAA-naïve

8-wk SOF/VEL/VOX did not meet criteria for noninferiority vs 12-wk SOF/VEL

Treatment difference: -3.4% (95% CI: -6.2% to -0.6%)

Slide credit: clinicaloptions.com

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
• Patient preference (8 or 12 w, # pills, packaging)

Our Case Patient

• 1a, start with 4 recommended regimens
  • resistance testing if elbasvir/grazoprevir only
• HIV neg
• Cirrhosis – no
  • Potentially eligible for 8 wk regimens
• Renal function normal so eligible all 4 regimens
• Medications:
  • Childbearing potential so avoid RBV
  • Anti-epileptics often have interactions
• Pills and packaging
  • Elbasvir/grazoprevir – 1 pill/d x 12 wks
  • Glecaprevir/pibrentasvir 3 pills/d x 8 wks
  • Sofosbuvir/ledipasvir x 8 wks
  • Sofosbuvir/velpatasvir x 12 wks

(WHAT PAYER COVERS)

Test all pregnant woman for HCV.
Remember to do pregnancy testing prior to treatment in women of childbearing potential
CASE 2 – When to do resistance testing and what to use in patients with ESRD

55 y.o. African American M with HIV (well controlled), HCV Geno 1b and cirrhosis, HCV RNA 221,000 IU/mL, ESRD on hemodialysis

HCV Hx:
- Treatment naïve
- Cirrhotic based on transient elastography measurement of 17 kpa
  - No decompensation events
  - EGD no varices
  - Sono no HCC

Other med Hx includes:
- HIV-infection on TDF, 3TC, and DOL
- HTN, high cholesterol, ESRD on hemodialysis
- Mild GERD on PPI qD
- HBV sAg- cAb+ sAb-, HBV DNA negative
### Recommended regimens listed by evidence level and alphabetically for:

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

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<th>GENOTYPE</th>
<th>DURATION</th>
<th>RATING</th>
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<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>1a, 1b, 4</td>
<td>12 weeks</td>
<td>I, B</td>
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<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)**</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>8 to 16 weeks**</td>
<td>I, B**</td>
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**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.

HCVguidelines.org accessed 9/29/17
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
Testing for HCV resistance (RASs) would be indicated in this patient with HCV geno 1b if…

1. He had failed PegIFN + RBV in the past
2. You plan to treat with 8 weeks of glecaprevir/pibrentasvir
3. You plan to treat with 12 weeks of grazoprevir/elbasvir
4. Nope! Resistance testing is not necessary here
5. Hmmm... What’s a RAS?
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Please enter the URL below.

https://api.event.com/polling/v1/api/polls/sptrdqg2

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
RAS Testing prior to Treatment

• NS5A RASs are relatively common (10-15%)
• Significance of NS5A RASs may depend on the RAS, 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 of G3 if cirrhosis

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RESULT COMMENT:
Mutations Detected: Q30R
REFERENCE RANGE:
HCV NS5a SUBTYPE: NOT DETECTED

This test was developed and its performance characteristics have been determined by Focus Diagnostics. Performance characteristics refer to the analytical performance of the test.

This test utilizes RT-PCR and DNA sequencing to detect the presence of treatment-emergent HCV NS5a variants associated with NS5a inhibitor antiviral therapy.

This assay is designed to amplify HCV genotypes 1a and 1b and may not successfully amplify other HCV genotypes.

This test was performed at: Focus Diagnostics, Inc., 33608 Ortega Highway, San Juan Capistrano, CA 92675

Resulting Agency: NEW YORK HOSPITAL LABORATORIES

Narrative
Hepatitis C Viral RNA NS5a Drug Resistance
22477X
FROZEN PLASMA
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

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
- Patient preference (8 or 12 w, # pills, packaging)

Our case patient
- 1b, no need for resistance testing, start with 4 recommended regimens
- HIV pos but no drug/drug interactions
- Cirrhosis – yes
  - No 8 wk regimens
  - Compensated so ok to use PIs
- Hemodialysis, no regimens w/ sofosbuvir, so 2 remaining regimens
- Medications: ARVs, PPI qd
  - Elbasvir/grazoprevir – no interaction
  - Glecaprevir/pibrentasvir (limit dose of PPI)
- Pills and packaging
  - Elbasvir/grazoprevir – 1 pill/d
  - Glecaprevir/pibrentasvir – 3 pills/d
- (WHAT PAYER COVERS)

HBV testing prior to treatment for all patients. Monitor for HBV reactivation during treatment if cAb+ (with DNA for sAg+ or DNA+, lfts/sx for others)
Continue cirrhosis management and HCC screening after cure
CASE 3 – Treatment and drug interactions in patients with HIV

49 y.o. M with HIV and HCV Geno 2, HCV RNA 120,000 IU/mL

HIV Hx:
   Well controlled on TDF/FTC + BID darunavir/ritonavir x 10 years

HCV Hx:
   Treatment naïve
   Fibroscan 6.1 kPa
   Acquired HCV 2 years ago – RF MSM

Other med Hx includes:
   HTN, renal insufficiency (CrCl 50)
   GERD on PPI
Which of the following regimens are recommended for genotype 2 infection in a person without cirrhosis?

1. Sofosbuvir/velpatasvir x 12 wks
2. Glecaprevir/pibrentasvir x 8 wks
3. Both 1 and 2
4. Neither 1 or 2
Insert Web Page

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Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/sp-3bjuf1

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
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
# Treatment Recommendations for Patients With HIV/HCV Coinfection

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>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 <a href="#">Initial Treatment of HCV Infection</a> and <a href="#">Retreatment of Persons in Whom Prior Therapy Has Failed</a>).</td>
<td>I, B</td>
</tr>
</tbody>
</table>

HCVguidlines.org accessed 9/29/17
Before administering sofosbuvir/velpatasvir in a patient with renal insufficiency (CrCl 50) on TDF/FTC + darunavir/ritonavir, which of the following should be considered?

1. Change darunavir/r dosing from BID to QD
2. Change TDF to TAF
3. Change darunavir/r to efavirenz
4. No ARV adjustment needed
Insert Web Page

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Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/sp-sb7tpw

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)

Sofosbuvir/velpatasvir can be used with most antiretrovirals, but not efavirenz, etravirine, or nevirapine. Because velpatasvir has the potential to increase tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min.

Due to limited experience with this drug combination, renal monitoring is recommended during the dosing period. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during sofosbuvir/velpatasvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy.
With SOF/LDV

TDF exposures are high in those on PIs

- TFV exposures are higher when TDF is coadministered with LDV/SOF compared to without LDV/SOF, but
  - Compared to the range of TFV exposures with available safety data
    - For EFV or RPV: TFV exposures fall within the range\(^1\)
    - For RTV-boosted PIs: TFV exposures partially exceed the range\(^2\)

---

Slide courtesy of J Kiser

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1. Data on File, Gilead Sciences.
3. German P, et al. ICPHHT 2014. #06
5. Chittick GE, et al. AAC. 2006; 50(4):1304-10 (SQV+RTV)
6. Zhu. 9th IWCPHT. 2008. #023 (ATV+RTV & LPV/r)

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

<table>
<thead>
<tr>
<th></th>
<th>SOF/LDV + TDF</th>
<th>SOF/VEL + TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CrCl &lt; 60 mL/min</strong>:</td>
<td>AVOID</td>
<td>AVOID</td>
</tr>
<tr>
<td><strong>CrCl &gt; 60</strong>:</td>
<td>MONITOR</td>
<td>MONITOR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>SOF/LDV + TDF + cobi- or ritonavir-boosted PI</th>
<th>SOF/VEL + TDF + cobi- or ritonavir-boosted PI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CrCl &lt; 60 mL/min</strong>:</td>
<td>AVOID</td>
<td>AVOID</td>
</tr>
<tr>
<td><strong>CrCl &gt; 60</strong>:</td>
<td>MONITOR or consider TAF</td>
<td>MONITOR or consider TAF</td>
</tr>
</tbody>
</table>

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

HCVguidlines.org accessed 9/29/17
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-Drug Interactions with DAAS

**Acid-reducing drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Elbasvir/Grazoprevir</th>
<th>Glecaprevir/Pibrentasvir</th>
<th>Ledipasvir/Sofosbuvir</th>
<th>Sofosbuvir/Velpatasvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

https://www.hep-druginteractions.org/
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall N=166</th>
<th>ARV Switch N=65</th>
<th>No Switch N=101</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Treatment Failure, n (%)</td>
<td>10 (6)</td>
<td>3 (5)</td>
<td>7 (7)</td>
<td>0.74</td>
</tr>
<tr>
<td>HIV viral failure</td>
<td>2 (1)</td>
<td>1 (1.5)</td>
<td>1 (1)</td>
<td>1.00</td>
</tr>
<tr>
<td>ARV switch</td>
<td>7 (4)</td>
<td>2 (3)</td>
<td>5 (5)</td>
<td>0.71</td>
</tr>
<tr>
<td>Development of AIDS</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>--</td>
</tr>
<tr>
<td>Change renal function, n (%)</td>
<td>48 (29)</td>
<td>14 (22)</td>
<td>34 (34)</td>
<td>0.11</td>
</tr>
<tr>
<td>Incident proteinuria</td>
<td>25 (15)</td>
<td>7 (11)</td>
<td>18 (18)</td>
<td>0.27</td>
</tr>
<tr>
<td>Creatinine &gt;0.4 mg/dL</td>
<td>12 (7)</td>
<td>6 (9)</td>
<td>6 (6)</td>
<td>0.54</td>
</tr>
<tr>
<td>Creatinine Clearance &lt;50 mL/min</td>
<td>19 (11)</td>
<td>5 (8)</td>
<td>14 (14)</td>
<td>0.32</td>
</tr>
<tr>
<td>SVR12 (N=153)</td>
<td>152 (99)</td>
<td>57 (100)</td>
<td>95 (99)</td>
<td>0.15</td>
</tr>
</tbody>
</table>
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
• Patient preference (8 or 12 w, # pills, packaging)

Our case patient
• 2, no need for resistance testing, start with 2 recommended regimens
• HIV pos – watch for drug interactions
• Cirrhosis – no
• CrCl 50, sofosbuvir ok but Cr Cl>30 but assess if TDF
• Medications: TDF, HIV PI, PPI qd need to be addressed
  • ARV adjustment needed
• Pills and packaging
  • Sofosbuvir/velpatasvir—1 pill/d
  • Glecaprevir/pibrentasvir 3 pills/d
• (WHAT PAYER COVERS)

Monitor MSM for reinfection at least annually.
Concept of HCV treatment as prevention has been proven for HIV+ MSM in Netherlands & Switzerland.
CASE 4 – Genotype 3 management

71 y.o. W with HCV Geno 3, HCV RNA 950,000 IU/mL

HCV Hx:
- Treatment naïve
- Fibroscan 14.2 kPa (c/w) cirrhosis
- No symptoms decompensation
- RAS testing: no mutations

Other med Hx includes:
- DM
- CrCL 55
Which of the following is recommended for initial treatment of HCV G3 in a patient with cirrhosis?

1. Sofosbuvir/ledipasvir x 12 wks
2. Sofosbuvir/velpatasvir x 12 wks
3. Elbasvir/grazoprevir x 12 wks
4. Glecaprevir/pibrentasvir x 8 wks
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Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/sp-h7ygo0

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
**G3 INITIAL TREATMENT RECOMMENDED REGIMENS**

**NO CIRRHOSIS:**
- Glecaprevir/pibrentasvir x 8 w
- Sofosbuvir/velpatasvir x 12 w
- Sofosbuvir + daclatasvir x 12w

**CIRRHOSIS:**
- Glecaprevir/pibrentasvir x 12 w
- Sofosbuvir/velpatasvir x 12 w*
- Sofosbuvir + daclatasvir +/- RBV x 24w*

*RAV testing for Y93H and add RBV if present or use sofosbuvir/velpatasvir/voxilaprevir
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
Glecaprevir/pibrentasvir and RASs -- 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 A30

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)

Most of this 3% w/ failure had cirrhosis

Figure S3B. By the Y93H NS5A resistance-associated variant (1% cutoff)

Total, n=274

Foster, NEJM, 2015, hcvguidelines.org
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
• Patient preference (8 or 12 w, # pills, packaging)

Our case patient
• Geno 3, 2 regimens, no A30K or Y93H present
• HIV neg
• Cirrhosis – yes
  • Compensated so PIs ok
• CrCl 55, sofosbuvir ok
• Medications: no drug interactions
• Pills and packaging
  • Sofosbuvir/velpatasvir – 1 pill/d x 12 wks
  • Glecaprevir/pibrentasvir 3 pills/d x 12 wks
• (WHAT PAYER COVERS)
It’s time!
Cure Everyone with HCV

- Remarkable advances in terms of HCV treatment tolerability & efficacy for patients with HIV
  - Recent advances in G2, G3, ESRD
  - SVRs for HIV/HCV very close to monoinfection
  - Still drug interaction issues, but valuable resources to help manage

- RAS testing prior to initial treatment if:
  - G1a and planned grazoprevir/elbasvir
  - G3 & cirrhosis and planned sofosbuvir/velpatasvir

- Successful treatment prevents cirrhosis, end stage liver disease, and hepatocellular cancer

- Post SVR – continue liver disease management/HCC screening, monitor HBV reactivation, and provide HCV RNA testing if ongoing risk
Resources

- HCVguidelines.org
- nynjaetc.org
- http://www.hep-druginteractions.org

THANK YOU