CASE STUDIES IN HEPATITIS C

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Goals

• THINK about hepatitis C therapy for every patient
  • Everyone is a candidate until proven otherwise
• Use available patient history and clinical data to triage patients for treatment now or treatment later
• Manage drug-drug interactions and adverse effects with telaprevir and boceprevir-based treatment
Evaluation of HIV/HCV: Goals

- Rule out acute HCV
- Assessment for advanced disease/cirrhosis
- Evaluation for contraindications to therapy with interferon, ribavirin or HCV protease inhibitors
  - Medical, psychiatric, social
- Education of patient about HCV
- Treat now or treat later?

History

- When were they diagnosed? Reason for testing?
- What was the risk factor? \( \text{duration of infection} \)
- Any history of ascites, GI bleeding, encephalopathy, easy bruising or bleeding, RUQ pain, edema, fatigue, elevated liver enzymes?
- Ever been treated before? If so, response
History: Focus on Contraindications to IFN

- Past Medical History: Autoimmune, Cardiac, Pulmonary problems
- Past psychiatric history
  - Hospitalizations, suicide attempts – how long ago?
  - Current control
  - Medications currently; do they see a psychiatrist?
- Medications: ALL
- Social: Drug and Alcohol Use, living situation
  - Consider Using AUDIT-C or similar

AUDIT-C

1. How often do you have a drink containing alcohol?
   0 Never
   1 Monthly or less
   2 2-4 times per month
   3 2-3 times a week
   4 4 or more times a week
AUDIT-C

2. How many standard drinks containing alcohol do you have on a typical day?
   0  1 or 2
   1  3 or 4
   2  5 or 6
   3  7 to 9
   4  10 or more

AUDIT-C

3. How often do you have six or more drinks on one occasion?
   0  Never
   1  Less than monthly
   2  Monthly
   3  Weekly
   4  Daily or almost daily

Men: >4, Women >3 identifies hazardous drinking or active alcohol use disorders
Physical Exam/Labs: Focus on Clues to Cirrhosis/Portal Hypertension

- Scleral Icterus
- Skin stigmata of portal hypertension: palmar erythema, caput medusae, spider angiomata
- Splenomegaly or palpable spleen
- Low platelets
- PT/INR
- HCV RNA not prognostic for fibrosis
- Imaging studies useful if positive, but not sensitive for cirrhosis
11/16/2012  GF  
41 BM  
HIV diagnosed 17 years ago  
HCV diagnosed 17 years ago, by routine screening after HIV dx  
No history of jaundice or other symptoms

Risk factor: IVDU once or twice, first in 1987  
No prior treatment

PMH: HIV, on tenofovir/emtricitabine/efavirenz since 1998  
Kaposi’s Sarcoma 2008 s/p chemotherapy

Prior psych history: None

Meds: tenofovir/emtricitabine/efavirenz  
doxycline 100 mg BID for acne

Social History:  
AUDIT-C score: 0  
Non smoker; sexually active with 1 woman 

Review of Systems + for back pain

Physical Exam:  
110/80    76    Weight 78.5 kg    BMI 26.3  
No scleral icterus, conjunctivae pink  
Heart and lungs normal  
Abdomen soft, liver span normal; no palpable spleen  
No palmar erythema, no caput medusae, no spider angiomata  
Remainder unremarkable
HCV RNA  69,000,000  
HCV genotype 1a/b mixed

Case 1: Assessment and Plan

• Estimated duration of infection 25-30 years (started IVDU in 1987, tested + for hepatitis C 17 years ago)
• No lab or PE evidence of advanced liver disease but this can be clinically silent
• No contraindications to HCV therapy identified in history or physical exam
• Patient decided to get liver biopsy to help determine urgency of treatment
Liver Biopsy Results

• Portal and periportal inflammation (Grade 1)
• Periportal fibrosis (Stage 1)
• 1+ iron

• Based on these findings, patient has elected to defer therapy until less toxic regimens with better efficacy are available.

Hepatitis C in HIV

• Faster progression to cirrhosis
• More fibrosis progression between paired liver biopsies
• Larger proportion of patients with advanced fibrosis compared to monoinfected populations
• Higher annual incidence of hepatic decompensation (~7%)
• Progression may be slowed by antiretroviral therapy, but data are conflicting
Serial liver biopsies in HIV+

<table>
<thead>
<tr>
<th>First biopsy fibrosis stage</th>
<th>Second biopsy fibrosis stage</th>
<th>Progression n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>85 (24%)</td>
</tr>
<tr>
<td>1</td>
<td>18</td>
<td>51 (22%)</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>17 (6%)</td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>19 (37%)</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2 (100%)</td>
</tr>
</tbody>
</table>

Median time between biopsies 2.9 years (IQR 2.3-3.4)
Only predictor of progression was ALT between biopsies

Sulkowski, AIDS 2007, 21: 2209-2216

Newer studies show HIV does not affect fibrosis progression rate

Interval between biopsies: 4.7 years (HIV+) vs 5.8 years (HIV-)

Sterling, Clin Gastro Hep, 2010; 8: 1070-76
FPR is related to HIV viral load

![Graph showing Fibrosis Progression Rate (IshFU/yr) with different CD4 counts and HIV RNA levels, indicating statistical significance with p-values.]

Brau, J Hep, 2006: 44: 47-55

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CASE 2
12/21/2012  BL  
46 WM  
HIV diagnosed 5 years ago  
HCV diagnosed 5 years ago, by routine screening after HIV dx  
No history of jaundice; only symptom is easy bleeding/bruising  

Risk factor: Sex with IVDU (MSM); multiple tattoos  
No prior treatment  

PMH: HIV, on Tenofovir/emtricitabine/rilpivirine  
which he just started  
Unspecifed colitis two months ago  

Prior psych history: History of depression and anxiety  
No history of hospitalizations for this  
Not on any medications for depression  

<table>
<thead>
<tr>
<th>Medications:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir/emtricitabine/rilpivirine</td>
</tr>
<tr>
<td>Oxycodone/acetaminophen 5/325 mg</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole one daily</td>
</tr>
</tbody>
</table>

Social History:  
**AUDIT-C score: 7**  
1 ppd since age 6; no past IDU; MSM, same partner x 10 years  

Physical Exam:  
108/70 72 Weight 72.1 kg BMI 21.2  
No scleral icterus, conjunctivae pink  
Heart and lungs normal  
Abdomen soft, liver span normal; no palpable spleen  
No palmar erythema, no caput medusae, no spider angiomata  
Remainder unremarkable
Total Protein 7.7
Albumin 4.3
Total Bilirubin 0.9
Alk phos 62
ALT 47
AST 38
PT 9.8
INR 0.8
CD4 160 (11%)
HIV viral load 48600

HCV RNA 17,100,000
HCV genotype 1a/b mixed
ANA 1:160

Case 2: Assessment and Plan

• No evidence of advanced liver disease by physical exam or labs
• More difficult in this case to estimate duration of infection
• There are several reasons why he is not a good candidate for treatment now:
  • HIV is not controlled
  • Substantial alcohol use
  • ?positive ANA
• Plan: counseled on cessation of all alcohol, continue antiretrovirals to increase CD4, reassess in 3 months
CASE 3

1/28/2013  DN
43 WM
HIV diagnosed in 1991
HCV diagnosed in 1993, by routine screening after HIV dx
No history of jaundice or other symptoms, except elevated LFTs

Risk factor: IVDU once in 1990s
No prior treatment

PMH: HIV
   Migraine headaches

Prior psych history: Depression; has been hospitalized twice, most recently in 2001; no suicide attempts; no current meds, but previously on fluoxetine
Medications:
- Tenofovir/emtricitabine + raltegravir
- Docusate
- Morphine sustained release 60 mg twice a day
- Cetirizine 10 mg daily as needed
- Milk thistle, licorice, N-acetyl cysteine

Social History:
- AUDIT-C score: 0
- 5 cigarettes/day

Physical Exam:
- 104/80  95  Weight 54.4 kg  BMI 19.4
- No scleral icterus, conjunctivae pink
- Heart and lungs normal
- Abdomen soft, liver span normal; no palpable spleen
  + palmar erythema, no caput medusae, +spider angiomata
- Remainder unremarkable

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Protein</td>
<td>8.1</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.4</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>0.6</td>
</tr>
<tr>
<td>Alk phos</td>
<td>78</td>
</tr>
<tr>
<td>ALT</td>
<td>68</td>
</tr>
<tr>
<td>AST</td>
<td>80</td>
</tr>
<tr>
<td>PT</td>
<td>14.3</td>
</tr>
<tr>
<td>INR</td>
<td>1.3</td>
</tr>
<tr>
<td>CD4</td>
<td>356 (17%)</td>
</tr>
<tr>
<td>HIV viral load</td>
<td>not det</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>1,640,000</td>
</tr>
<tr>
<td>HCV genotype</td>
<td>3a</td>
</tr>
</tbody>
</table>
Case 3: Assessment and Plan

- Estimated duration of infection 20+ years
- Palmar erythema, spider angioma, low-ish platelets, and INR of 1.3 suggest that he may have advanced disease/cirrhosis
- He has genotype 3a, which affects choice of HCV treatment (no protease inhibitor) and response rates
- He is reluctant to have either a biopsy or undergo treatment
- Decide to do noninvasive test of fibrosis

Results of Noninvasive Testing

- Fibrosis score 0.74 consistent with cirrhosis

Given advanced disease, patient now considering treatment with peginterferon and ribavirin; pre-emptive antidepressant being considered given his history of depression

Ioannou, Hepatology 2013; 57:249-257

Dotted lines represent prevalence adjusted by direct standardization to the age distribution of the entire population from all calendar years.


Ioannou, Hepatology 2013; 57:249-257

Dotted lines represent prevalence adjusted by direct standardization to the age distribution of the entire population from all calendar years.
Trends in the Prevalence of HCC in HIV-Infected Veterans 1996-2009

Dotted lines represent prevalence adjusted by direct standardization to the age distribution of the entire population from all calendar years.

Ioannou, Hepatology 2013; 57:249-257

Treatment decreases risk of death or liver-related complications

Fernandez-Montero, AASLD 2012, #946
Health Maintenance for Cirrhotics

- Surveillance for hepatocellular carcinoma
  - US (+/- AFP) every 6 months
  - MRI to follow up abnormalities
- EGD to screen for esophageal varices
  - Especially if there are other signs of portal hypertension
- Counseling to avoid raw oysters (*Vibrio vulnificus*)
- Awareness for other complications of cirrhosis
  - Encephalopathy
  - Ascites

CASE 4
12/24/12 KS
50 WM
HIV diagnosed 1984
HCV in 2008 because of elevated ALT to 1800s with acholic stools and flu-like illness consistent with acute hepatitis C; prior HCV antibody in 2001 was negative

Risk factor: MSM

Was treated for acute hepatitis C – had severe fatigue, could not work during that time due to fatigue; Had a partial EVR but never went to undetectable and had a viral breakthrough on treatment; no dose reductions, but he had some anemia, and had to take erythropoietin injections

PMH: HIV, dx 1984
Chronic fatigue syndrome
HSV-2, on acyclovir suppression

Prior psych history: None

Meds:
Tenofovir/emtricitabine + raltegravir
Modafinil 200 mg daily
Diphenoxylate-atropine 2 tabs BID
Pregabalin 200 mg BID
Acyclovir 400 mg BID
Triamcinolone nasal spray

Social History:
AUDIT-C score: 1
Non smoker; sexually active with men
Physical Exam:
112/76  78  Weight 82.9  BMI 27.7
No scleral icterus, conjunctivae pink
Heart and lungs normal
Abdomen soft, liver span normal; no palpable spleen
No palmar erythema, no caput medusae, no spider angiomata
Remainder unremarkable

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<tbody>
<tr>
<td>142</td>
<td>106</td>
<td>17</td>
<td>103</td>
<td>4.6</td>
<td>28</td>
<td>1.20</td>
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<tr>
<td>5.9</td>
<td>14.4</td>
<td>230</td>
<td>39.0</td>
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</tbody>
</table>
Case 4: Assessment and Plan

- Known date of infection: 5 years duration
- Low likelihood of advanced disease
- Two options:
  - Retreat with protease inhibitor based therapy
  - Wait for better options
- Patient worried because he couldn’t work the last time he was treated and cannot afford to be off work now
- Anemia on treatment also worrisome – will be worse with protease inhibitors
- He decided to defer for new therapies, perhaps as part of a study

Rapid Progression After Acute HCV Infection in HIV+ MSM

- 4 patients who acquired HCV via sexual transmission
- All with HIV, controlled on ART
- 1 treated with Peg/RBV in acute setting, but failed; other 3 declined treatment
- Initial biopsies:
  - Pt 1: stage 3 at 8 months after infection
  - Pt 2: stage 2 at 4 months after infection
  - Pt 3: stage 3 at 4 years after infection
  - Pt 4: stage 3 at 4.5 years after infection
Rapid Progression after Acute HCV

- Developed decompensated ESLD 17 months to 6.5 years after acute infection

Outcomes:
- Pt 1: transplanted 2 years after infection
- Pt 2: died, 2.75 years after infection
- Pt 3: died, 8 years after infection
- Pt 4: died, 7 years after infection

CASE 5
HIV diagnosed 1989
HCV diagnosed in 1989 on routine testing; no history of jaundice; no manifestations of end-stage liver disease; asymptomatic

Risk factor: IVDU, first use ~1978, has been clean for 4-5 years

Treated with Peg/ribavirin from 3/26/2010 to 6/2011 (56 weeks) and had relapse. During treatment, she had severe anemia, and ribavirin was held for about 2.5 months, then restarted for a short period, then permanently d/c’d about month 7. She needed erythropoeitin injections, and required transfusions on several occasions. She lost a lot of weight (from 160 pounds to 94 pounds)

PMH: HIV, dx 1989
Asthma, controlled without inhalers
2 clipped aneurysms in brain

Prior psych history: Depression – hospitalized 7-8 years ago; anxiety; on quetiapine and trazodone; no psych problems on treatment the first time

Tenofovir/emtricitabine + lopinavir/ritonavir
Quetiapine 200 PO BID gabapentin 300 mg TID
trazodone 150 mg daily ranitidine 300 mg daily
Bupropion 150 mg daily dronabinol 5 mg TID
Amitriptyline 50 mg daily buprenorphine/naltrexone
TMP-SMX 1 daily 8 mg/2 mg daily

AUDIT-C score: 1
Clean 5-6 years; 5-6 cigs/day
Physical Exam:
120/78 72 Weight 59.8 kg BMI 21.9
No scleral icterus, conjunctivae pink
Heart and lungs normal
Abdomen soft, liver span normal; no palpable spleen
No palmar erythema, no caput medusae, no spider angiomata
Remainder unremarkable

136 104 18
4.9 27 0.69

12.1
4.5
37.2
153

Total Protein 8.3
Albumin 3.3
Total Bilirubin 0.2
Alk phos 92
ALT 21
AST 28
PT 12.1
INR 1.0
CD4 204 (15%)
HIV viral load not det
HCV RNA 5,690,000
HCV genotype 1

Liver biopsy 10/16/2012: Grade 3 portal inflammation; stage 4 fibrosis (cirrhosis); 1+ iron stain
Case 5: Assessment and Plan

- Established cirrhosis by biopsy, but compensated (MELD 6)
- Prior relapser to Peg/ribavirin with significant side effects (dose reductions may have affected response)
- Drug-drug interaction between HCV protease inhibitors and lopinavir-ritonavir
  - Needs antiretrovirals changed if treatment considered
- Although treatment will be challenging, decided to attempt
  - ARVs changed to tenofovir/emtricitabine/raltegravir
  - Anticipate dose reduction of ribavirin

Antiretroviral Regimens that are OK with HCV Protease Inhibitors

<table>
<thead>
<tr>
<th>Antiretroviral Regimen</th>
<th>HCV Protease Inhibitor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telaprevir</td>
<td>Atazanavir</td>
</tr>
<tr>
<td></td>
<td>Efavirenz (need higher TPV dose)</td>
</tr>
<tr>
<td></td>
<td>Raltegravir</td>
</tr>
<tr>
<td>Boceprevir</td>
<td>Raltegravir</td>
</tr>
<tr>
<td></td>
<td>Atazanavir*</td>
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<tr>
<td></td>
<td>Efavirenz*</td>
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<tr>
<td></td>
<td>?Darunavir</td>
</tr>
<tr>
<td></td>
<td>?Lopinavir/ritonavir</td>
</tr>
</tbody>
</table>

*Recommended to avoid in package insert, but generally accepted as safe

Also studied:
- **Dolutegravir**: no interactions
- **Maraviroc**: dose 150 mg BID, as TPV and BOC triple drug concentrations
  - No recommendations if MRV also used with HIV protease inhibitors
    - (which also triple MVC concentrations)
- **Rilpivirine** and BOC: no dose adjustments
# Drugs Contraindicated with HCV PIs

<table>
<thead>
<tr>
<th>TELAPREVIR</th>
<th>BOCEPREVIR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfuzosin</td>
<td>Alfuzosin</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Carbamazepine, phenobarbital, phenytoin</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Cisapride</td>
<td>Ergot derivatives</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Cisapride</td>
</tr>
<tr>
<td>Lovastatin, simvastatin</td>
<td>St. John’s wort</td>
</tr>
<tr>
<td>Sildenafil or tadalafil when used for PAH</td>
<td>Lovastatin, simvastatin</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Drosperinone</td>
</tr>
<tr>
<td></td>
<td>Sildenafil or tadalafil when used for PAH</td>
</tr>
<tr>
<td></td>
<td>Triazolam</td>
</tr>
</tbody>
</table>

# Drug Interactions with HCV PIs

<table>
<thead>
<tr>
<th>TELAPREVIR</th>
<th>BOCEPREVIR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone, bepridil, flecainide, propafenone, quinine, digoxin, lidocaine</td>
<td>Amiodarone, bepridil, flecainide, propafenone, quinine, digoxin</td>
</tr>
<tr>
<td>Coumadin</td>
<td>Coumadin</td>
</tr>
<tr>
<td>Clarithromycin, erythromycin</td>
<td>Trazodone, desipramine</td>
</tr>
<tr>
<td>Carbamazepine, phenobarbital, phenytoin</td>
<td>Azoles: itra, keto, vori, posa</td>
</tr>
<tr>
<td>Trazodone, escitalopram</td>
<td>Colchicine</td>
</tr>
<tr>
<td>Azoles: keto, itra, posa, vori</td>
<td>Clarithromycin, rifabutin</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Felodipine, nifedipine, nicardipine</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Inhaled budenoside, fluticasone, salmeterol</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Bosentan</td>
</tr>
<tr>
<td>Amlodipine, diltiazem, felodipine, nicardipine, nifedipine, nisoldipine, verapamil</td>
<td>Atorvastatin</td>
</tr>
<tr>
<td>Prednisone, methylprednisolone, dexamethasone</td>
<td>Cyclosporine, Tacrolimus, sirolimus</td>
</tr>
<tr>
<td>Inhaled or nasal fluticasone, budesonide, salmeterol</td>
<td>Methadone, buprenorphine</td>
</tr>
<tr>
<td>Bosentan</td>
<td>Ethinyl estradiol</td>
</tr>
<tr>
<td>Atorvastatin, fluvastatin, pravastatin, rosuvastatin</td>
<td>Alprazolam</td>
</tr>
<tr>
<td>Ethinyl estradiol, nortindrone</td>
<td>PDE5 inhibitors: sildenafil, vardenafil, tadalafil</td>
</tr>
<tr>
<td>Cyclosporine, tacrolimus, sirolimus</td>
<td></td>
</tr>
</tbody>
</table>
### Drug Interactions with HCV PIs

**TELAPREVIR**
- Amiodarone, bepridil, flecainide, propafenone, quinine, digoxin, lidocaine
- Coumadin
- Clarithromycin, erythromycin
- Carbamazepine, phenobarbital, phenytoin
- Fosinopril, metoprolol, propranolol
- Ketorolac, indomethacin
- Lidocaine
- Amoxicillin
- Azithromycin
- Ciprofloxacin
- Fluconazole
- Methylprednisolone
- Dexamethasone
- Sildenafil, vardenafil
- Tadalafil
- Bosentan
- Alprazolam
- Methadone
- Methimazole
- Ethinyl estradiol, nortriptyline, doxepin
- Cyclosporine, Tacrolimus, sirolimus
- Methadone, buprenorphine
- PDE5 inhibitors: sildenafil, vardenafil, tadalafil

**BOCEPREVIR**
- Amiodarone, bepridil, flecainide, propafenone, quinine, digoxin
- Coumadin
- Trazodone, desipramine
- Azoles: keto, itra, vori, posa
- Colchicine
- Clarithromycin, rifabutin
- Felodipine, nifedipine, nicardipine, nisoldipine, verapamil
- Dexamethasone
- Inhaled or nasal fluticasone, budesonide, salmeterol
- Bosentan
- Atorvastatin, fluvastatin, pravastatin, rosuvastatin
- Ethinyl estradiol, nortriptyline
- Cyclosporine, tacrolimus, sirolimus
- Repaglinide
- Methadone
- PDE5 inhibitors: sildenafil, vardenafil, tadalafil

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### Case: Treatment Initiation

- Despite poor tolerance of treatment the first time, she has cirrhosis (well-compensated) and wants to try again with protease-inhibitor
- ARVs changed to Truvada + raltegravir
- Other meds OK
- Because of expected anemia, telaprevir chosen over boceprevir due to shorter duration (12 weeks vs 44 weeks)
Week 3

- Subjective: nausea, can’t eat very much; + fatigue
- Objective: -0.5 kg since beginning of treatment; physical unchanged

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th>Hb</th>
<th>Hct</th>
<th>Plts</th>
<th>HCV RNA</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>2.7</td>
<td>11.3</td>
<td>34.5</td>
<td>102</td>
<td>5,690,000</td>
</tr>
<tr>
<td>Week 3</td>
<td>3.1</td>
<td>9.1</td>
<td>27.6</td>
<td>103</td>
<td></td>
</tr>
</tbody>
</table>

**ACTION:** Decrease ribavirin to 600 mg (400 mg in AM, 200 mg in PM), repeat labs in 1 week

Anemia can occur early

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*Jacobson, NEJM 2011; 364: 2405-16*
**Anemia Management**

- For Hb<10, decrease ribavirin to 200 mg-400 mg
- For Hb<8.5, discontinue ribavirin
- If ribavirin held for >14 days, protease inhibitor must also be discontinued
- Ribavirin may be restarted at lower dose
- No dose reductions for TPV or BOC
- +/- adding erythropoietin-stimulating agent
### Week 4

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th>Hb</th>
<th>Hct</th>
<th>Plts</th>
<th>HCV RNA</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>2.7</td>
<td>11.3</td>
<td>34.5</td>
<td>102</td>
<td>5,690,000</td>
</tr>
<tr>
<td>Week 3</td>
<td>3.1</td>
<td>9.1</td>
<td>27.6</td>
<td>103</td>
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<tr>
<td>Week 4</td>
<td>3.1</td>
<td>8.1</td>
<td>25.5</td>
<td>107</td>
<td>Not det</td>
</tr>
</tbody>
</table>

**ACTION:** Begin darbepoeitin injections weekly, with weekly CBCs

Could not get in touch with patient to tell her to come in for injection; letter sent; finally got it after a week delay

### Week 6

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th>Hb</th>
<th>Hct</th>
<th>Plts</th>
<th>HCV RNA</th>
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<td>Baseline</td>
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<td>34.5</td>
<td>102</td>
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</tr>
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<td>25.5</td>
<td>107</td>
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<tr>
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<td>3.1</td>
<td>7.4</td>
<td>22.7</td>
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</tbody>
</table>

**ACTION:** Hold ribavirin, type and screen for transfusion; repeat darbepoeitin injection
Week 7

• Subjective: Weak and cold; fatigued, can barely stay awake; continued weight loss; mood OK, occasional leg cramps
• Objective: another -5.4 kg weight loss
• To get transfusion in clinic today
• No post-transfusion H&H obtained because patient arrived too late in the day
• Return to clinic 1 week

Week 8

• Subjective: Fatigue better, coldness better; appetite slightly improved
• Objective: weight +0.5 kg from last visit; PE unchanged

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th>Hb</th>
<th>Hct</th>
<th>Plts</th>
<th>HCV RNA</th>
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<tbody>
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<td>7.4</td>
<td>22.7</td>
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<td>31.2</td>
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ACTION: Darbepoetin injection, restart ribavirin at 200 mg daily, CBC in 1 week
Through Week 18

- Has completed telaprevir phase
- Ribavirin had to be discontinued due to ongoing anemia
- Hemoglobin stable around 8.5
- Wk 12 HCV RNA not detected
- Wk 17 HCV RNA not detected
- Has lost 37 pounds since starting treatment
  - Boost, Marinol

CASE 6
10/2/12 CS
41 WM
HIV diagnosed 2008
HCV diagnosed in 2008 on routine testing; no history of jaundice; no manifestations of end-stage liver disease; asymptomatic

Risk factor: nasal cocaine, first use 1985

Past psych history: Anxiety; depression since age 16 but never hospitalized; suicide attempt when he was a teenager; attempted OD after a breakup in 2004

Meds: tenofovir/emtricitabine/efavirenz
diazepam 1 mg bid prn
citalopram 20 mg daily

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<th>Total Protein</th>
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<tr>
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</table>
TREATMENT INITIATION → WEEK 4

- Started on peginterferon and ribavirin
- At week 4 visit, has lost 2.3 kg, having trouble with appetite, having myalgias and cramping after injection
- Has been more emotional and irritable
- Works at convenience store, sometimes throws mop/snow shovel or yells at customers when it gets busy
- No suicidal ideation; +crying spells

ACTION: increase citalopram to 40 mg daily

WEEK 8

- Subjective: Still decrease appetite, but gained +0.8 kg since last visit
- Still very irritable; having temper tantrums at grocery store – his parents will no longer take him out in public
- Very emotional – cried at the Oscars and the Grammys, even though he was watching them in public
- Uncontrollable diarrhea

ACTION: Refer to mental health, loperamide prn for diarrhea
Week 20

• Has been seeing mental health
• Reiki treatments helping irritability
• HCV RNA at weeks 4 and 12 not detected
• Planning 24 weeks of treatment
  • Had RVR and baseline viral load low; genotype 3

Psychiatric Side Effects

• Baseline assessment of psych history
• Consider pre-emptive SSRI
• Baseline CES-D (Centers for Epidemiologic Studies Depression Scale)
• CES-D at every treatment visit to monitor for changes
• Asking about mood
• Also ask spouse, sig other, people who are around patient (if they come to the visit)
CES-D

- [http://www.chcr.brown.edu/pcoc/cesdscale.pdf](http://www.chcr.brown.edu/pcoc/cesdscale.pdf)
- 20 questions
- Scored 0-60, with higher scores indicating more symptomatology
- Trend over time

Managing Psych side effects

- Adding SSRIs
- Trazodone for sleep
- Referral to psychiatry
- May lead to therapy discontinuation
11/30/12  
45 W MTF transgender  
CD4 987, viral load undetectable  
Prior relapser to Peg/RBV  
Biopsy: Grade 2/Stage 2  
Genotype 1a  

Week 26  
Peginterferon alfa-2b 150 mcg weekly  
Ribavirin 600 mg BID  
Boceprevir 800 mg q8 hours  

HCV RNAs:  
Baseline: 8,490,000  
Week 4: 4,400 (end of lead-in)  
Week 8: <25  
Week 12: <25  
Week 24: <25
Week 26

- Patient came to ED stating that her roommate “is trying to kill her” but cannot state why or how
- Having visual hallucinations of a little girl crying in the corner of her bedroom
- Also auditory hallucinations of babies crying
- No suicidal or homicidal ideation
- Patient admitted to hospital for further eval

Hospital eval

- Urine tox screen and blood ethanol negative (except for prescribed meds)
- TSH, CK normal
- BMP, hepatic panel normal
- WBC 1.9, Hb 9.3, Hct 30.4, Plts 92
- CT head with generalized atrophy without focal abnormality
- The next morning, pt has no recollection of the events described in ED
- Last thing she recalls is throwing away hep C meds because she “couldn’t take it anymore”
Follow Up

- All hepatitis C therapy was stopped
- No recurrence of delirium/psychosis
- Patient is awaiting post-therapy evaluation of HCV RNA – maybe enough therapy for SVR?

Rash management (telaprevir)

- Good general skin care
- Assess severity and extent (BSA involved)
- Antihistamines, emollients for pruritus
- Topical corticosteroids (start with lower potency and work up)
- Mild and moderate rashes – continue drug with frequent follow up
- Severe – discontinue telaprevir
- Systemic corticosteroids are not recommended
Rash management

- Ribavirin can cause rash too!
  - If rash doesn’t resolve off TPV, may need to d/c Peg/RBV
- Systemic symptoms (DRESS), Stevens-Johnson, TEN, erythema multiforme have been described (including fatal cases)
  - Discontinue all therapy immediately
  - May need admission to hospital for specialty care

QUESTIONS??