Acute to Chronic Hepatitis C

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JUNE 3, 2014

Patient History

- 52 yo Hispanic male with HCV and HIV coinfection
- Developed acute hepatitis in December 2012
  - Found as part of quarterly HIV lab monitoring
  - Patient had asymptomatic elevations of AST/ALT
  - Baseline October AST/ALT: 24/22 IU/L
  - December AST/ALT: 122/182 IU/L
  - One week later AST/ALT: 650/1013 IU/L
Past Medical History

- HIV diagnosed in 1992
  - CD4 850 cells/cmm
  - HIV RNA undetectable <40 copies/mL
- Candidal esophagitis
- Anxiety, depression and insomnia
- Chronic pain
- Constipation
- H/o cocaine and heroin dependence
- Heavy tobacco user

Medications

- Tenofovir/emtricitabine (Truvada), raltegravir (Isentress), and lopinavir/ritonavir (Kaletra) as HAART
- Mirtazapine, trazodone, and quetiapine for mood and sleep
- Gabapentin and etodolac for pain
- Docusate and polyethylene glycol for constipation
- No known allergies
Labs

- 1 week after initial abnormal LFTs in December 2012
  - Known immunity to hepatitis A, with positive total IgG/IgM from 1990s
  - Hepatitis B surface Ag, sAb & coreAb negative
    - Failed HBV vaccination
  - Hepatitis C Ab weakly positive
  - HCV RNA 2.5 million IU/mL
  - HCV Genotype 1a and 1b

Social History

- Patient divulges, after positive drug screen, that he had relapsed with IV heroin, at the time of the acute hepatitis
- Eventually agreed to outpatient rehabilitation
- Eager to have HCV treated, and always adherent to HAART
  - Planned to start PegIFN + ribavirin, but he relapsed again
12 Months Later

- Finally ready to start therapy
- Clean from all substances, except tobacco, for 5 months
- Now has chronic hepatitis C
- Had previously ordered PegIFN and ribavirin
- Decided to add sofosbuvir (Sovaldi) to this regimen based on new treatment guidelines
- Pre-treatment AST/ALT now 85/140 IU/L
- HCV RNA now 1.4 million IU/mL

Sofosbuvir

- An NS5b hepatitis C polymerase inhibitor
- Once daily, single tablet
- FDA-approved for use in HIV/HCV coinfection
- High resistance barrier
- Can be used with:
  - PegIFN + ribavirin
  - Simeprevir +/- ribavirin
  - Ribavirin without interferon
HCV Lifecycle and STAT-C (Specifically Targeted Antiviral Therapy for Patients with HCV)


Treatment Plan

- Started PEG-interferon, weight-based ribavirin and once-daily sofosbuvir
- Two weeks into therapy
  - Hospitalized with insomnia, irritability, diarrhea and uncontrolled rectal pain
  - ALT 40 IU/L, down from 140 IU/L in 2 weeks
  - HCV RNA < 12 IU/mL at 2 weeks, though still detected
    - HCV RNA down from 1.4 million IU/mL at start of therapy
  - Colonoscopy showed internal hemorrhoids and mild rectal prolapse only
  - Pain controlled on multiple therapies for pain, including tramadol
Polymerase and NS5A Inhibitors

- HCV protease inhibitors have historically been response-guided

- Polymerase and NS5A inhibitors are not response-guided

- Might be other reasons to consider HCV RNA at 2 – 4 weeks
  - Adherence measure
  - Reassurance to patient
  - Reassurance to provider

NEUTRINO Study

- The phase 3 NEUTRINO trial evaluated sofosbuvir (400 mg daily) in combination with PEG-IFN alfa 2a 180 mcg by subcutaneous injection weekly) and weight-based RBV (1000 mg to 1200 mg daily) for 12 weeks in 291 treatment-naive patients with chronic HCV genotype 1 infection.

- The SVR12 for patients with genotype 1 infection was 89%.
  - SVR12 did not differ substantially by baseline characteristics

- SVR 12 was lower in patients with cirrhosis (80%) than in those without cirrhosis (92%).

P7977-1910 HIV/HCV CoInfection Study

- A single-center, single-arm trial (N=23) investigating this same 12-week triple therapy regimen in HIV+ patients coinfected with HCV genotypes 1, 2, 3, or 4
- Allowable antiretrovirals included either efavirenz, atazanavir/ritonavir, darunavir/ritonavir, raltegravir or rilpivirine in combination with tenofovir/emtricitabine
- 21 patients (91%) with GT1 achieved SVR 12
- 2 patients discontinued early due to anemia and altered mood


Patient Follow-UP

- Hospitalized a second time for rectal pain
  - Pelvic CT scan normal
- HCV RNA undetected at week 6
- Week 10 presented with worsening mood, irritability and crying
  - PEG-IFN discontinued
  - Finishing out his 12-week course of sofosbuvir and ribavirin
- Challenges with his sofosbuvir refills, unrelated to insurance
Sofosbuvir Key Points

- 400mg tablet, once daily dosing, with no food restrictions

<table>
<thead>
<tr>
<th>HCV Mono-infected and HCV/HIV Co-infected</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 or 4</td>
<td>Sofosbuvir + Peg-interferon + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 2</td>
<td>Sofosbuvir + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>Sofosbuvir + ribavirin</td>
<td>24 weeks</td>
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</tbody>
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Take-Home Points

- 1) Sofosbuvir therapy is not response-guided
- 2) Mental health assessment at baseline and ongoing is still important.
- 3) Specific therapy and treatment course have to be individualized