Hepatitis C
Case-Based Scenarios
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Case 1: Victor

- 50 year old Mexican male
- HCV diagnosed in 1995
- Former IDU heroin user, last use 1996
- Treatment naïve, fearful of treatment
- History of anxiety
- GT 2B
- Baseline HCV RNA: 6,432,020 IU/mL
What does Victor need next?

- Liver Biopsy?
- Psychological evaluation?

Liver Staging and HCV Treatment

- Biopsy rarely needed
- Not required in Genotypes 2 and 3, given SVR >80%
- If patient is motivated to be treated, and biomarkers and imaging show no evidence of cirrhosis, can treat without biopsy
- Non-invasive methods can be used to stage, to determine who can defer treatment
- Fibroscan helpful if available
- APRI index uses Platelets and AST
Psychological Preparation for HCV Treatment

- The Psychosocial Readiness Evaluation and Preparation for Hepatitis C Treatment (PREP-C)
- Initial assessment of a patient’s psychosocial readiness to begin HCV treatment.
- prep.c.org

HCV Treatment GT 2 and GT 3 Current Standard of Care

- Peg IFN alfa 2a 180mcg/mL sc weekly or Peg IFN alfa 2b 1.5 mcg/kg sc weekly
- Ribavirin 800 mg daily
  Duration : 24 weeks

(If co-infected, treat x 48 weeks)
### HCV RNA Trend

<table>
<thead>
<tr>
<th>Time point</th>
<th>Baseline</th>
<th>WK 4</th>
<th>WK 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV RNA (IU/mL)</td>
<td>6,432,020</td>
<td>1,560</td>
<td>ND*</td>
</tr>
</tbody>
</table>

ND = Not Detected

### Treatment HCV RNA Trend

- **Baseline**: 6,432,020 IU/mL
- **Week 4**: 1,560 IU/mL
- **Week 12**: ND
- **Week 24**: ND

HCV RNA IU/mL
Other Important Laboratory Values:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>14.4 g/dL</td>
<td>12.6 g/dL</td>
<td>11.0 g/dL</td>
</tr>
<tr>
<td>Plats</td>
<td>184 K</td>
<td>156 K</td>
<td></td>
</tr>
<tr>
<td>ANC</td>
<td>2.1 x 10^3</td>
<td>1.9 x 10^3 (lowest)</td>
<td></td>
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</tbody>
</table>

ALT/AST

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>64/ 73 IU/L</td>
<td>13/20* IU/L</td>
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</table>

*Biochemical response

Side Effects and Management

- **Anorexia:**  
  Small frequent meals, smoothies

- **Dry skin:**  
  Ammonium lactate lotion, increased hydration

- **Fatigue, irritability:**  
  Took a break from gym routine, and attended yoga  
  Monthly visits with psychologist
Post Treatment F/u

- End of Treatment HCV RNA
- 4 weeks post treatment
  - Monitor for continued SE’s
  - Check CBC
- Week 12 SVR
- Week 24 official SVR check
  *Victor remained ND and was ND at his last F/u in August 2013

Lisa

- 59 yo AA female with HIV/HCV co-infection
- HIV Stable on tenofovir, emtricitabine, atazanavir/ritonavir
- HCV treatment naive
- HX depression
- NO ETOH or drug use
- Prior cocaine and marijuana use, last use 12 yrs ago
Baseline Labs

- CD4 914 cells/cmm
- HIV RNA 67 copies/mL
- HCV RNA 12,099,408 IU/mL
- HGB 12.4 g/dL; Platelets 142,000
- ALT 33, AST 61 IU/L; TB 0.6 g/dL
- CR 1.33 mg/dL
- AFP 1.2 ng/mL

Do any of these values suggest cirrhosis?

Abdominal Ultrasound

- 6/22/11
- IMPRESSION:
  - Echogenic liver, with a minimally nodular contour consistent with cirrhosis
  - No intrahepatic mass is identified
Additional Work-up

- Fibroscan score 19.3 kpa - Stage F4
- EGD - no varices
- Nephrology consult given elevated creatinine 1.3-1.5 mg/dL
- Stage 2-3 proteinuric kidney disease, likely familial
  - Started lisinopril, and told to avoid NSAIDS
  - Tenofovir/emtricitabine discontinued, & replaced with abacavir/lamivudine
- Psych clearance, given hx of substance abuse and depression

Triple Therapy Started

- TVR 750 mg PO TID with fatty food (20 g)
- Peg IFN alfa 2 a sc q week
- RBV 1000mg daily
  *Creatinine clearance at baseline = 55.4 mL/minute
  RBV dose adjustment if Cr Cl 30-50 mL/minute

TVR and PEG IFN - no renal dose adjustment
Week 4

- Week 4 of HCV Treatment
- C/o fatigue
- Shortness of breath after walking up stairs or >5 blocks
- Daily nausea. Some relief with metoclopramide
- Is taking TVR with fatty food.
  - Denies missing any doses.

Rapid Hemoglobin Drop

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>ED (next day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb g/dL</td>
<td>12.4</td>
<td>11.2</td>
<td>8.1</td>
<td>7.3</td>
</tr>
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</table>
Anemia Interventions

- Ribavirin held
- Patient phoned and instructed to go to ED for transfusion
- Arrived following day with HGB 7.3
- Transfused to 9.2
- Erythropoietin started (40,000 unit sc q wk)
- Weekly CBCs thereafter

HCV RNA

- Baseline: 12,099,408 IU/mL
- Week 4: Non-detectable (RVR)
- Week 12: Non-detectable (eRVR)
Importance of eRVR

- In treatment-naïve patients achieving eRVR, 92% achieved SVR
- If eRVR achieved, high baseline HCV RNA did not influence SVR
- eRVR allows for shortened treatment duration in mono-infected HCV patients

Close Monitoring and Medication Titration
Ensure Safety and Response

- 2 weeks later → Hgb 10 g/dL
- RBV resumed at 200 mg daily
- Patient continues TVR, PEG IFN and EPO
- Wk 8 HCV RNA Still ND; HGB 8.2 g/dL, Cr 1.78 mg/dL - CR CL 41 mL/min; RBV held; transfused
- Wk 12 HCV RNA ND, TVR completed; HGB 9.1 g/dL
- Wk 14 HGB 10.8 g/dL
  - RBV reintroduced at 200mg daily
Treatment Completed

- EOT (End of treatment) response: HCV RNA ND
- Has had WK 12 post-treatment response
- Hgb 11 g/dL
- Creatinine continues to be elevated at 1.45 mg/dL
- Return for WK 24 post-treatment assessment

SVR 12 vs SVR 24

- Clinical Guidelines - HCV RNA 24 weeks after completion of treatment to determine SVR
- 2011 FDA accepted SVR 12 as endpoint for clinical trials
- HCV relapse usually occurs within first 12 weeks after the EOT
- SVR 12 can be used with a 99.7% positive predictive value for predicting SVR 24
- SVR 24 should still be obtained as confirmation
Case 3: Michael

53 yo caucasian male with HCV
- Former IDU - heroin user
- 1995 HCV DX
- 2006 Prior relapser to PEG IFN/ RBV; developed severe anemia during treatment, required dose reductions
- Cirrhosis as per liver biopsy 2008

Relevant Labs
- HGB 15.8 g/dL;
- Plat 138 K
- AFP 15.6 ng/mL
- ALT 88/ AST 125 IU/L
- TB 0.9 mg/dL
- ALB 4.0 g/dL
Additional Work-up

- CT scan: liver normal in size, & no masses
- EGD - grade 1 esophageal varices

Medications

- Nadolol
- Omeprazole
- Lovastatin
- Citalopram
- Quetiapine
- Clonazepam

Would any of these be contraindicated with BOC or TVR?
Medication Change

- Lovastatin discontinued
- Rosuvastatin started

GT 1 Treatment with Boceprevir

- Peg IFN weekly
- RBV 1200mg daily

Lead-in x 4 weeks, then add:
- Boceprevir 800mg (4x 200mg caps)
  PO TID
Week 4

- Pt having fatigue, body aches, & poor appetite
- Mild depression and feelings of aggression
- Reports perfect adherence to treatment

Mental Health Management

- Psychiatric follow up monthly
- Psychiatric medication doses may need to be increased while on interferon
- Psychologist monthly or p.r.n. if symptoms are exacerbated
How many weeks of treatment are warranted?

Despite early response, remember with TVR and BOC based triple therapy:

- If co-infected, treat x 48 weeks
- If cirrhotic treat x 48 weeks
Anemia Intervention WK 24

- RBV reduced by 50%
- Erythropoietin started
- 2 weeks later = Hgb 10.5 g/dL
- RBV dose reduction does not affect SVR rates in BOC or TVR-based triple therapy

Case 4: Juan

- 32 yo HIV + Colombian male
- Stable on abacavir/epivir+ atazanavir/ritonavir
- CD4 680 cells/cmm; HIV VL ND
- MSM
- Methamphetamine abuser
- November 2012: AST 19; ALT 22 IU/L
- March 2013: AST 745; ALT 1214 IU/L
Sexual History

- Has 2 regular male partners
- "Nonchalant" about condom use; usually used only with the HIV negative partner
- Believes HIV + partner fools around
- Anal receptive intercourse
- Recalls one episode of unprotected anal intercourse with a one-night stand 4 months ago while high

Acute HCV Diagnosed

- HCV AB +
- HCV RNA 520,332 IU/mL
- GT 1A
- Abdominal US normal
- ALT 160; AST 57 IU/L by time of referral
**Acute HCV Clinical Guidelines**

- Can delay treatment for up to 12 weeks after suspected onset of HCV, to allow for spontaneous resolution.
- Should ideally treat within 6 months of acute infection for optimal response.
- PEG-IFN and RBV is recommended by most expert panels.
- Length of treatment 24 weeks in mono-infection, & 48 weeks in co-infection.

**Telaprevir in Acute HCV**

- Open label pilot study in co-infected MSMs.
- TVR, Peg IFN and RBV x 12 weeks.
- 17 out of 20 patients (85%) had undetectable HCV RNA at the end of treatment and SVR4 at 4 weeks post-treatment.
- Among participants with longer follow-up, 82% (14 out of 17) achieved SVR12 and 79% (11 out of 14) reached SVR24.
- No relapses occurred among people with end-of-treatment response.

D Flierer. Telaprevir for Acute Hepatitis C Virus in HIV+ Men both Shortens Treatment and Improves Outcome. 20th Conference on Retroviruses and Opportunistic Infections. Atlanta, March 3-6, 2013.
Juan’s Side Effects

- Nausea, anorexia
- Anorectal irritation
- Day 7 - develops rash to arms and chest and severe generalized pruritis

SE Management

- Nausea: metoclopramide
- Perianal burning: hydrocortisone/pramoxine per rectum
- Rash:
  - cetirizine
  - hydrocortisone 2.5% lotion
HCV RNA

- Baseline 1.2 million IU/mL
- Week 2 <43 IU/mL
- Wk 4 Not Detected
- Wk 12 Not Detected

Response and Lessons Learned

- End of Treatment response achieved
- WK 12 post treatment: Still not detected
- AST/ALT WNL
- No methamphetamine use since began treatment
- Using condoms
- Our work does not end with cure!
- Prevent re-infection: education and harm reduction.
References

- Slides 20, 36 - An Update on Treatment of Genotype 1 Chronic Hepatitis C Virus Infection: 2011 Practice Guideline by the American Association for the Study of Liver Diseases HEPATOLOGY, Month 2012