Initiation of Hepatitis C Treatment: A Prescriber’s Guide

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✓ I have no conflict disclosures
✓ I will discuss therapies under investigation

Step 1 – Need for Treatment?

Confirm diagnosis HCV status
Assess liver status
Assess comorbidities

Step 2 – Is your patient ready?

Ready, Willing, Able?
Likelihood of Success
Contingency Plan
### Current (On Label) Standard of Care Treatment

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Agents</th>
<th>Duration</th>
<th>SVR 12/18 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sofavi (SOF), Ribavirin (RBV), Peg-Interferon alfa (PEG)</td>
<td>12 weeks</td>
<td>60% SVR12/60% SVR18w</td>
</tr>
<tr>
<td></td>
<td>Olysio (SMV), Ribavirin (RBV), Peg-Interferon alfa (PEG)</td>
<td>24 or 48 weeks</td>
<td>60% SVR12/60% SVR18w</td>
</tr>
<tr>
<td>2</td>
<td>Sofavi (SOF), Ribavirin (RBV)</td>
<td>24 weeks</td>
<td>90%</td>
</tr>
<tr>
<td>3</td>
<td>Sofavi (SOF), Ribavirin (RBV), Peg-Interferon alfa (PEG)</td>
<td>12 weeks</td>
<td>90% SVR12</td>
</tr>
<tr>
<td>4</td>
<td>Sofavi (SOF), Ribavirin (RBV), Peg-Interferon alfa (PEG)</td>
<td>12 weeks</td>
<td>97%</td>
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</tbody>
</table>

### Current Off-Label Uses

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### Treatment Notes
- On-treatment monitoring as with previous treatment regimens
- RBV: dosing is weight-based
- Sofavi: dose reduction for anemia (no effect on SVR)
- Check HCV RNA at treatment week 4
- Do not use in GFR <30
- No stopping rules (only relapses were observed)
- Significant drug/drug interactions with SMV (follow package insert)
- Check HCV RNA at treatment weeks 4, 12, and 24
- Discontinue if >25,000 IU/ml

### New Options

**IFN-free for gt1**

- Genotype 1
  - Sofavi (SOF)
  - Ribavirin (RBV)
  - Peg-interferon alfa
  - Duration: 12 weeks
  - SVR: 90% overall (NEUTRINO) 80% cirrhotics
  - Treatment notes:
    - Simeprevir given for the first 12 weeks only
    - 10% diminished response in genotype 1a Q80K polymorphism
    - 24 weeks for prior relapse or treatment naïve
    - 48 weeks for prior partial and null response

**IFN-free for gt1 or 4**

- Genotype 1 or 4
  - Sofavi (SOF)
  - Ribavirin (RBV)
  - Peg-interferon alfa
  - Duration: 12 weeks
  - SVR: 98 – 100% (COSMOS) 90% in GT 1a Q80K (add RBV)
  - Treatment notes:
    - Check HCV RNA at treatment weeks 4, 12, and 24
    - Discontinue if >25,000 IU/ml

**Genotype 2/3**

- Sofavi (SOF)
- Ribavirin (RBV)
- Duration:
  - Genotype 2: 12 weeks
  - Genotype 3: 24 or 48 weeks
- SVR: 90%

**Genotype 4**

- Sofavi (SOF)
- Ribavirin (RBV)
- Peg-interferon alfa
- Duration: 12 weeks
- SVR: 97%

### Co-infection

- HCC, pre-transplant

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Upcoming Regimens (Fall 2014)

- Abbvie
  - Gt 1 only (SVR12: 95 – 98%)^3
  - 5 drugs:
    - Protease inhibitor/ritonavir/NS5A fixed dose combination (FDC) daily
    - Non-nucleoside/tide polymerase inhibitor (BID)
    - RBV (BID)
- Gilead
  - Gt 1 (SVR 95% – 100%)^2, 3
  - SOF(NS5B)/ledipasvir(NS5A) FDC daily

Success on Treatment

- Motivation
- Information
- Medication Adherence
- Self Efficacy
- Social support and Stability
- Alcohol and Substance Use
- Psychiatric Stability
- Energy Level
- Cognitive Functioning

Cirrhosis

- No contraindication for SOF in cirrhosis
  - No data on SOF in GFR <30 (don’t use)
- Intrahepatic levels of SMV are increased in cirrhosis:

| Child's A | ↑ 1.3 - 2.8 fold |
| Child's B | ↑ 2.4 fold |
| Child's C | ↑ 5 fold |

- SMV contraindicated in Child's B and C cirrhosis
- BMS compassionate use Daclatasvir protocol (IRB Pending)
Challenges our Patients Face

- Stigma of Hepatitis C
- Psychiatric & Substance Use Comorbidity
- Adherence
- Drug-Drug Interactions
- HCV Treatment side effects

Exclusion criteria or Characteristics of the Patient Population?

Challenges our Patients Face

- Social instability
- Family issues/disclosure
- Coverage
- Logistics, eg:
  - Ability to receive packages
  - Refrigeration

Hepatitis C Treatment Readiness: Case Study #1

- 55 year old man with bipolar disorder
- Genotype 1b
- Non-cirrhotic
- Prior treatment elsewhere in 1998
  - TIW IFN + ribavirin
  - Did not complete treatment
Hepatitis C Treatment Readiness: Case Study #1

- Prior treatment:
  - Became irritable
  - Stabbed someone with an ice pick
  - Arrested, spent one month at Bellevue

- Pre-treatment baseline
  - Court-ordered anger management program
  - Outside psychiatrist Q2 months
  - Seroquel, citalopram

10 – 15% of individuals with bipolar disorder have chronic HCV infection

Success on IFN therapy if

- Assessed meticulously
- Observed carefully
- Followed extensively
- Similar rates of on-treatment psych complications

Riff, 2006, J Clin Psychiatry
Kelly et al. 2012 Eur J Clin Diabetes & Hep
Hepatitis C Treatment Readiness: Case Study #1

- Coordinated with:
  - Psychiatrist
  - Therapist assigned
  - Insomnia: Seroquel vs liver
- Agrees to give his ice pick to a friend to hold
  - Security of the HCV team
  - Came in for weekly injections
  - Seen weekly by our mental health team

- Missing mid-day boceprevir dose
  - Thought it needed to be refrigerated
  - u/d at treatment week 8→36-week course

- While on treatment:
  - Psychiatrist “getting rid of him”
  - Death of parent
  - Charity fund needed to bridge Seroquel
  - “Honor your doctor” donations
  - March, 2014: SVR-16

To Treat or Not to Treat?
Treat now
or
Treat later?

Hepatitis C Treatment Readiness:
Case Study #2

- Fetal alcohol syndrome
- Bipolar depression
- Borderline personality disorder
- Frequent psych admissions
  - Admitted after IFN-related suicidal ideation
  - Offered to resume while inpatient

Hepatitis C Treatment Readiness:
Case Study #2

- 56-year old female
- Risk: IDU; age 18
- Genotype 1a
- Treated 2004 peg/riba:
  - Stopped at TW 4 for suicidal ideation
- Since then: confirmed progression to cirrhosis
- HCV-related RA arthralgias

Hepatitis C Treatment Readiness:
Case Study #2

- Continuity of primary care
- Psych care now elsewhere
- Involved daughter
Hepatitis C Treatment Readiness: Case Study #3
- 42-year old male
- Genotype 3a
- Ukrainian
- Undocumented
- hepCAP

Hepatitis C Treatment Readiness: Case Study #4
- 56 year old female
- Genotype 1a, IL28-B = TT
- Risk nasal cocaine, age 28
- Vs Ab- → Ab+ in ~2002/3
- Biopsy history:
  - 2004: grade 1-2, stage 0
  - 2010: grade 1, stage 1
- Treatment naïve

Hepatitis C Treatment Readiness: Case Study #3
- PMHx: alcohol
- Platelets: 44
- Abdominal ultrasound:
  Echogenic nodular liver, compatible cirrhosis. No focal sonographically detectable hepatic mass. Detectable hepatic mass. Further assessment may be obtained with contrast-enhanced CT scan or MRI.

Hepatitis C Treatment Readiness: Case Study #4
- Asthma
- HTN, hyperlipidemia, DM2
- Chronic uveitis
- Chronic β-thal anemia
- Renal cell carcinoma
  - Partial right nephrectomy 2013
  - GFR = 40’s
Hepatitis C Treatment Readiness: Case Study #5

- 36-year old male
- Genotype 1a
- Recently released from prison
- Risk: IDU x 1, age 20; some nasal drug use until age 30
- No signs of significant cirrhosis/fibrosis

Hepatitis C Treatment Readiness: Case Study #5

- Family supportive

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Hepatitis C Treatment Readiness: Case Study #6

- 54-year old pre-op m/f transgender
- Genotype 1a
- Risk: Hormone injections starting age 20; some nasal drug use
- No signs of significant cirrhosis/fibrosis

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Hepatitis C Treatment Readiness: Case Study #5

- 6 years in prison
- Lives in a program
  - Getting help with housing
  - Looking for a job
  - On Medicaid during transition
- No medical comorbidities
- Mild depression/anxiety/insomnia r/t prison stay
Hepatitis C Treatment Readiness: Case Study #6
- No major comorbidities
- Anxiety not treated with medications

Hepatitis C Treatment Readiness: Case Study #6
- Lives nearby with elderly mother
  - Has not disclosed
  - Concerned about worrying her
- Concerned about appearance
- Work:
  - Had been working without coverage
  - Lost job, became Medicaid eligible

Hepatitis C Treatment Readiness: Case Study #7
- 23-year old male
- Attending college
- Sexually acquired
  - 3 months ago
  - Endorsed previous negative test
  - HCV+ sexual partner actively menstruating/HSV outbreak
  - Has since infected his girlfriend

Hepatitis C Treatment Readiness: Case Study #7
- No comorbidities
- Lives 200 miles away
  - Chose Mount Sinai
  - Asks for:
    - Rx for medical marijuana
    - Letter so he can withdraw from classes
    - Needs to move off campus with girlfriend for support
Thank you