Use of Ribavirin in Current DAA regimens

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Disclosures

• I have received research grant support to UCSF related to HCV from Abbvie, Bristol-Myers Squibb, Gilead, Merck, & Pfizer
Case #1

- 48 year old man, HCV GT2, no cirrhosis
  - COPD, well controlled, no O2 requirement
- Female partner, s/p tubal ligation
Role of ribavirin

Function: may help to reduce development of resistance & augment response in treatment experienced and cirrhotic patients

• Genotype 2 & 3: RBV still commonly used (GT2>3)
• Genotype 1: limited role
  – Genotype 1A: Required with PrOD (“Viekira Pak”)
  – Optional: Shorten therapy in cirrhotic, treatment experienced
• Use in treatment of some of hardest to treat populations: decompensated cirrhotics & DAA treatment failures
### RBV in Genotype 2

<table>
<thead>
<tr>
<th>Population</th>
<th>Regimen</th>
<th>Compensated Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naïve</td>
<td>• SOF + Ribavirin x 12 weeks&lt;br&gt;• <em>(SOF + Daclatasvir x 12 weeks)</em>&lt;br&gt;• <em>(SOF + PEG/RBV x 12 weeks)</em></td>
<td>Extend SOF+RBV to 16 weeks if cirrhotic</td>
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<tr>
<td>PEG/RBV treatment experienced</td>
<td>• SOF + RBV x 16-24 weeks&lt;br&gt;• <em>(SOF + PEG/RBV x 12 weeks)</em></td>
<td></td>
</tr>
</tbody>
</table>

### RBV in Genotype 3

<table>
<thead>
<tr>
<th>Population</th>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naïve</td>
<td>• SOF + Daclatasvir x 12 weeks&lt;br&gt;• <em>(SOF + Ribavirin x 24 weeks)</em></td>
<td>Extend SOF + Daclatasvir to 24 weeks and consider adding RBV if cirrhotic</td>
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<tr>
<td>PEG/RBV treatment experience</td>
<td>• SOF + Daclatasvir x 12 weeks&lt;br&gt;• <em>(SOF + PEG/RBV x 12 weeks)</em></td>
<td>Extend SOF + Daclatasvir to 24 weeks and add RBV if cirrhotic</td>
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# RBV in GT 1

<table>
<thead>
<tr>
<th>Population</th>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GT1a</strong></td>
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<tr>
<td>GT1 a treated with PrOD (“Viekira pak”)</td>
<td>• PrOD + RBV x 12 weeks (non cirrhotic) or 24 weeks (cirrhotic)</td>
<td>Caution with PrOD in cirrhosis</td>
</tr>
<tr>
<td><strong>Cirrhotic patients</strong></td>
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<td></td>
</tr>
<tr>
<td>Cirrhotic (treatment naïve or experienced)</td>
<td>SOF + Daclatasvir +/- RBV x 24 weeks</td>
<td>Unclear if RBV required in cirrhotics. Not FDA approved</td>
</tr>
</tbody>
</table>
| Cirrhotic, treatment experienced (PEG/RBV +/- HCV PI) | • Sofosbuvir/Ledipasvir + RBV x 12 weeks or  
  • Sofosbuvir/Ledipasvir without RBV x 24 weeks | Either regimen acceptable                                                 |
| Decompensated cirrhotics        | • Sofosbuvir/ledipasvir or SOF+DCV + low dose RBV (600 mg daily) x 12 weeks | Decompensated cirrhotics should be managed in consultation with expert   |
| **Prior treatment failures**    |                                                                         |                                                                          |
| Prior treatment failure with SOF+RBV (+/- PEG) | Sofosbuvir/ledipasvir + RBV x 12 weeks (non-cirrhotic) or x 24 weeks (cirrhotic) | NS5a failures or sofosbuvir/simeprevir failures should be managed in consultation with an expert |
Ribavirin dosing & side effects

• Dosing
  – 1200 mg for ≥ 75 kg, 1000 mg for < 75 kg, divided BID
  – 600 mg if “low dose” – titrate up if tolerated
  – Caution in CrCL < 50: dose reduction required

• Side effects
  – Hemolytic anemia - variable degree,
    • Can be accompanied by elevated indirect bilirubin
  – Rash
  – Insomnia
  – Teratogenicity: both for men & women, avoid pregnancy x 6 months post exposure

• Drug interactions & contraindications
  – AZT
  – CrCL < 30 – challenging to manage
  – Patients who cannot tolerate potential for anemia - serious heart or pulmonary disease, baseline anemia that cannot be remedied
## Monitoring on Ribavirin

| Prior to therapy | • CBC, renal function  
• Assessment for diseases that may be exacerbated by anemia (CAD, severe pulmonary disease, etc.)  
• Assessment for pregnancy potential (men & women) |
|------------------|--------------------------------------------------------------------------------------------------|
| On RBV           | • Q 2 week CBC for first 6 weeks, monthly thereafter if stable  
• Monitor renal function if impaired at baseline  
• Regular contraceptive counseling & pregnancy testing if indicated |
| Dose reduction   | • If history of CAD or other concern about poor tolerance of anemia, dose reduce if Hgb drops > 2 g/dl over 4 weeks  
• Otherwise, dose reduce at Hgb < 10 g/dl  
• Hold for Hgb < 8.0  
• Dose reduction preferred to EPO  
*Would discuss with HCV expert if anemia during SOF+RBV regimen- avoid SOF monotherapy* |
Back to the case

• 48 year old man, HCV GT2, treatment naïve, non cirrhotic
  – COPD- moderate, but well controlled
  – Female partner: s/p tubal ligation

• 12 weeks of Sofosbuvir + Ribavirin (600 mg BID for weight of 80 kg)

• Clinical course:
  – Baseline Hgb: 13 g/dl
  – Week 2: 11 g/dl; QD iron started
  – Week 4: 9 g/dl-> dose reduced to 600 mg/d, HCV < LLOQ
  – Week 5: 9.5 g/dl: no action, q 2 week CBC
  – Week 7: 9.0 g/dl
  – Week 9: 9.3 g/dl
  – Completed HCV tx, week 12 post treatment HCV < LLOD (SVR12) and Hgb 12 g/dl
Take homes

• Goal is to avoid RBV when possible but RBV can be given effectively and safely in those who need it
• Close monitoring for anemia
• Dose reduction generally not associated with lower cure rates
  – Avoid DAA monotherapy- if anemia threatens ability to continue RBV, discuss with HCV expert
• Avoid pregnancy/fathering a child x 6 months after RBV exposure