TREATMENT OF HCV DECOMPENSATED CIRRHOSIS

Mitchell L Shiffman, MD
Director
Liver Institute of Virginia
Bon Secours Mercy Health
Richmond and Newport News, VA
## ML SHIFFMAN
### DISCLOSURE OF CONFLICTS

<table>
<thead>
<tr>
<th>Company</th>
<th>Roles</th>
<th>Company</th>
<th>Roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbvie</td>
<td>Advisor, Grant, Speaker</td>
<td>Gilead</td>
<td>Advisor, Grant, Speaker</td>
</tr>
<tr>
<td>Bayer</td>
<td>Advisor, Speaker</td>
<td>Intercept</td>
<td>Advisor, Grant, Speaker</td>
</tr>
<tr>
<td>Bristol Myers-Squibb</td>
<td>Advisor, Grant, Speaker</td>
<td>Immuron</td>
<td>Grant</td>
</tr>
<tr>
<td>Conatus</td>
<td>Grant</td>
<td>Merck</td>
<td>Grant, Advisor, Speaker</td>
</tr>
<tr>
<td>CymaBay</td>
<td>Grant</td>
<td>NGMBio</td>
<td>Grant</td>
</tr>
<tr>
<td>Daiichi Sankyo</td>
<td>Speaker</td>
<td>Novartis</td>
<td>Grant</td>
</tr>
<tr>
<td>Dova</td>
<td>Advisor, Speaker</td>
<td>Optum Rx</td>
<td>Consulting</td>
</tr>
<tr>
<td>Exalenz</td>
<td>Grant</td>
<td>Salix</td>
<td>Advisor, Speaker</td>
</tr>
<tr>
<td>Galectin</td>
<td>Grant</td>
<td>Shire</td>
<td>Grant</td>
</tr>
<tr>
<td>Genfit</td>
<td>Grant</td>
<td>Shionogi</td>
<td>Advisor,</td>
</tr>
</tbody>
</table>
HCV DECOMPENSATED CIRRHOSIS CASE

• 2001:
  - Chronic HCV diagnosed age 54 years
  - Risk: Blood transfusion following MVA age 16 years
  - LBX in 2001: Stage 2 fibrosis, platelet count 175,000
  - HCV genotype 1A, HCV RNA Log 6.2 IU
  - PEGINF-2a 180 mcg QW, Ribavirin 1200 mg QD
• 2016 (Now age 69 years):
  - Treatment stopped at week 12
  - Variceal bleeding treated with band ligation
  - Developed edema, ascites, HE
  - Paracentesis. Step 1 diuretics.
  - Lactulose BID
HCV DECOMPENSATED CIRRHOSIS CASE

- Two weeks after hospital discharge:
  - No obvious ascites/edema, grade 1 HE
  - TBILI 2.5 mg/dl (42 umol/L), ALB 3.3 g/dL (33 g/L)
  - NA 136, Scr 1.2 mg/dl (106 umol/L), NH3 60 umol/L
  - HB 10 g/dl (100 g/L), PLT 85,000, INR 1.5
  - AFP 5.7 ng/ml, AFP-L3 12%
  - Ultrasound. Cirrhosis, no mass, patent PV, mild ascites
  - CTP 9, Child Class B, MELD 17
# HCV DECOMPENSATED CIRRHOSIS OPTIONS

<table>
<thead>
<tr>
<th>Pros</th>
<th>Treat HCV</th>
<th>Liver Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cure HCV</td>
<td>Eliminate cirrhosis</td>
</tr>
<tr>
<td></td>
<td>• Improve liver function</td>
<td>Eliminate risk of HCC</td>
</tr>
<tr>
<td></td>
<td>• Reduce risk of HCC</td>
<td>Higher HCV cure after LT</td>
</tr>
<tr>
<td></td>
<td>• Avoid transplantation</td>
<td></td>
</tr>
<tr>
<td>Cons</td>
<td>Lower cure rate</td>
<td>Prior to transplant:</td>
</tr>
<tr>
<td></td>
<td>Risk of HCC persists</td>
<td>• Disease progression</td>
</tr>
<tr>
<td></td>
<td>Symptoms of cirrhosis</td>
<td>• Risk of decompensation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of HCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of never getting a LT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-LT:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Immune suppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other post-LT complications</td>
</tr>
</tbody>
</table>
HCV DECOMPENSATED CIRRHOSIS TREATMENT ISSUES

• Agents containing protease inhibitors cannot be used
  – Glecaprevir-piprentasvir
  – Sofosbuvir-velpatasvir-voxalaprevir
  – Elbasvir-grazoprevir
• Response rates lower than with no decompensation
• Using ribavirin increases SVR
• Complications of cirrhosis may interrupt treatment
HCV DECOMPENSATED CIRRHOSIS DURATION OF THERAPY

HCV DECOMPENSATED CIRRHOSIS
ROLE OF RIBAVIRIN

All patients treated 12 weeks

SVR (%)

LDV/SOF
DCV/SOF
SOF/VEL

Ribavirin
- Yes
- No

CHILD CLASS: A-17%, B-73%, C-10%

B: 100%

HCV DECOMPENSATED CIRRHOSIS DISEASE SEVERITY

All patients treated 12 weeks

SVR (%)

LDV/SOF+RBV

DCV/SOF+RBV

CHILD Class

A

B

C

HCV DECOMPENSATED CIRRHOSIS
LOWER SVR THAN AFTER LT

HCV DECOMPENSATED CIRRHOSIS
SVR IMPROVES LIVER FUNCTION

Mean change: -1.2
Median change: -1

Mean change: -1.7
Median change: -2

M Charlton et al.
Gastroenterol. 2015; 149:649-659.
### HCV DECOMPENSATED CIRRHOSIS
DELISTING OF PATIENTS WITH SVR

<table>
<thead>
<tr>
<th>MELD</th>
<th>ΔMELD &lt;2</th>
<th>ΔMELD 2-4</th>
<th>ΔMELD &gt;4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16</td>
<td>9/33 = 27%</td>
<td>12/14 = 86%</td>
<td>4/4 = 100%</td>
</tr>
<tr>
<td>16-20</td>
<td>2/19 = 11%</td>
<td>2/12 = 17%</td>
<td>3/7 = 43%</td>
</tr>
<tr>
<td>&gt;20</td>
<td>0/8 = 0%</td>
<td>0/1 = 0%</td>
<td>2/4 = 50%</td>
</tr>
</tbody>
</table>

- Liver Institute of Virginia
- Bon Secours Mercy Health
- LS Belli et al
# HCV DECOMPENSATED CIRRHOSIS OPTIONS

<table>
<thead>
<tr>
<th>Pros</th>
<th>Treat HCV</th>
<th>Liver Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cure HCV</td>
<td>Eliminate cirrhosis</td>
</tr>
<tr>
<td></td>
<td>• Improve liver function</td>
<td>Eliminate risk of HCC</td>
</tr>
<tr>
<td></td>
<td>• Reduce risk of HCC</td>
<td>Higher HCV cure after LT</td>
</tr>
<tr>
<td></td>
<td>• Avoid transplantation</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cons</th>
<th>Treat HCV</th>
<th>Liver Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower cure rate</td>
<td>Prior to transplant:</td>
</tr>
<tr>
<td></td>
<td>Risk of HCC persists</td>
<td>• Disease progression</td>
</tr>
<tr>
<td></td>
<td><strong>MELD purgatory</strong></td>
<td>• Risk of decompensation</td>
</tr>
<tr>
<td></td>
<td>• Cure SVR</td>
<td>• Risk of HCC</td>
</tr>
<tr>
<td></td>
<td>• Disease progression halted</td>
<td>• Risk of never getting a LT</td>
</tr>
<tr>
<td></td>
<td>• MELD remains 16-20</td>
<td>Post-LT:</td>
</tr>
<tr>
<td></td>
<td>• Cirrhosis symptoms persist</td>
<td>• Immune suppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other post-LT complications</td>
</tr>
</tbody>
</table>
FRANS FRANCKEN. MAN CHOOSING BETWEEN VIRTUE AND VICE 1633.

Liver Transplant

MELD PURGATORY

Death from Complications of Cirrhosis
MELD PURGATORY
Modern Era Leader Dysfunction
HCV DECOMPENSATED CIRRHOSIS CASE

- Treated with Sofosbuvir-velpatasvir QD
  - Did not want to use RBV because HB 10 gm
  - Planned for 24 weeks of treatment
  - HCV RNA undetectable at week 4 and 12
  - Hospitalized with pneumonia, stage 4 HE at week 14
  - Physicians did not want to place NG tube because of previous variceal bleeding
  - Did not take DAA for 5 days
  - HCV RNA recurrence
  - Treatment stopped
HCV DECOMPENSATED CIRRHOSIS FAILING DAA TREATMENT

HCV DECOMPENSATED CIRRHOSIS CASE

• Evaluated and placed on LT waiting list with MELD 17
  - Agreed to accept an HCV positive donor
• Monitored every 3 months
  - Repeat EGD varices. Banding performed
  - Ultrasound to screen for HCC every 6 months
• 2017 (age 70 years)
  - 3 cm mass on routine ultrasound
  - AFP 121, L3 33%
  - Dynamic MRI 3.2 cm enhancing mass, with washout and delayed rim enhancement, right lobe, segment 6.
Patients with more advanced cirrhosis have a lower SVR and a higher rate of developing HCC. 8% vs 4% per year

GN Iounnou et al
HCV DECOMPENSATED CIRRHOSIS
RISK OF NEW HCC AFTER DAA

- 1927 patients
- SVR in 95%
- 2 years monitoring
- 161 had prior HCC with HCC recurrence rate of 25%
- De Novo HCC developed in 2.8%
- Strongest predictors of HCC
  - No SVR
  - Esophageal varices

A Lleo et al.
EASL 2018; PS-154
HCV DECOMPENSATED CIRRHOSIS CASE

- HCC treatment
  - TACE. 3 month MRI. Residual enhancement.
  - MWA. 3 month MRI. No enhancement. No new lesions.
- 2018 (age 71 years)
  - Mild muscle wasting
  - Step 2 diuretics, Lactulose and xifaxan
  - TBILI 3.3 mg/dl (56 umol/L), ALB 3.0 g/dl (30 gm/L)
  - NA 133, Scr 1.4 mg/dl (124 umol/L), NH3 55 umol/L
  - HB 12.0 g/dL (120 g/L), PLT 85,000, INR 1.5
  - MRI. No enhancing mass, patent PV, mild ascites
  - CTP 10, Child Class C, MELD 23
HCV DECOMPENSATED CIRRHOSIS CASE

- Treated with sofosbuvir-velpatasvir, ribavirin 600 mg QD for 12 weeks
- Achieved SVR
- 2019 (age 72 years)
  - No recurrence of HCC
  - Performance status improved
  - CTP 7, MELD 18
  - Removed for LT waiting list
  - Continues to be screened for HCC recurrence
HCV DECOMPENSATED CIRRHOSIS
ADVERSE EVENTS AFTER SVR

Adverse events:
- Death
- HCC
- Liver transplant
- Decompensation
- Sepsis
- All cause hospitalizations

MCM Cheung et al.  
HCV DECOMPENSATED CIRRHOSIS IMPROVEMENT IN PROs WITH SVR

ZM Younossi et al
HCV DECEOMPENSATED CIRRHOSIS SUMMARY

Patients with HCV decompensated cirrhosis are the most difficult to manage.
They are not hard to treat.
They simply have too much baggage.

Child Class B and C makes these patients slower.
The SVR is about 10% lower.
If hospitalized during treatment this may prevent closure.
And the use of a PI is just not Kosher.
HCV DECEOMPENSATED CIRRHOSIS
SUMMARY

We thought we were rid of Ribavirin
But in decomp cirrhosis leaving it out is a sin
So we reluctantly retreat to a place we had been
To maximize SVR and achieve a big win

Treat or wait till OLT
Is the big question in decomp C
The risk is landing in place called MELD purgatory
Where HCV is cured but that’s not the key
Because the patient feels bad and is in constant misery
Just hoping to develop a small HCC
So a liver transplant can set them free
HCV DECEOMPENSATED CIRRHOSIS
SUMMARY

But in patients who feel good and the MELD score is low
DAA treatment should be a go
Patients with SVR are happy…. Ho, Ho, Ho
The HCC risk declines and that makes us crow
And quality of life improves as measured by PRO

So managing HCV in decomp cirrhosis
Can lead you to develop neurosis
So step back and carefully consider the prognosis
Before you choose the option that’s bogus