Hepatitis C Update: Approach to the New Therapies

Stanley Martin Cohen M.D.
Professor of Medicine
Medical Director, Hepatology

University Hospitals Case Medical Center
Case Western Reserve School of Medicine
Cleveland, Ohio
Disclosures

● Grants/Research Support
  – Bristol-Myers Squibb

● Consultant
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● Speakers’ Bureau
  – Bristol-Myers Squibb, Gilead Sciences

● Stock Shareholder
  – None

● Other Financial or Material Support
  – None

● I will be speaking outside of the standard FDA recommendations.
Impact of Hepatitis C

Liver transplant
- HCV is the #1 cause of liver transplant in the United States
- Up to 45% of patients awaiting liver transplant have HCV

Liver cancer
- HCV is the leading cause of HCC

Death
- 4% annual death rate postcirrhosis
- CDC has identified the number of deaths from HCV now exceed those from HIV

Deaths Due to HCV Now Exceed HIV Deaths

Mortality due to HCV infection may be vastly under-estimated due to under-reporting on death certificates.

Chronic HCV in the US: Underdiagnosed and Untreated

Estimated treatment rate is based on Q2 and Q4 2011 chart audits.

Prevalence: 4.1 M
Diagnosed: 1.6 M
Treated: 89

Unaware of Infection: 38%
Treated: 5.5%
AASLD Recommendation: HCV Screening and Testing

- All persons should be screened for behaviors that place them at high risk for HCV infection
- Persons who are at risk should be tested for the presence of HCV infection
  - Injected illegal drugs (past and current)
  - Selected medial conditions
  - Prior recipients of transfusions or organ transplants
  - Children born to HCV-infected mothers
  - Health care, emergency medical and public safety workers after needle sticks, sharps, or mucosal exposure to HCV-positive blood

New Screening Guidelines

- CDC has issued draft guidelines recommending a one-time anti-HCV antibody test for all baby boomers (those born from 1945 through 1965).

- USPSTF agreed with a level B recommendation.

Risk-cohort screening  birth-cohort screening

Effectiveness of HCV Testing for Persons Born during 1945-1965 – Summary Results from 3 Randomized Trials

- Evaluated Birth Cohort Screening strategies in 3 randomized trials
- Compared the frequency of HCV diagnoses using BCT to risk-based SOC
- More patients tested for HCV in all intervention arms with BCT

**Center A**
- Randomize
  - Patient Letter
    - Tested for HCV 27% vs 1.4%
    - N= 2996
  - Control
    - Tested for HCV 1.4%
    - N= 5996

**Center B**
- Randomize
  - Provider Alert
    - Tested for HCV 31% vs 3.6%
    - N= 8313
  - Control
    - Tested for HCV 3.6%
    - N= 5168

**Center C**
- Randomize
  - Recruiter
    - Tested for HCV 60%
    - N= 4608
  - Control
    - Tested for HCV 3.6%
    - N= 10,358

**Pooled Results**
- RR=8.0 (95%CI 1.7-37.7)
- RR=3.2 (95%CI 1.3-7.8)
- RR=5.2 (95%CI 2.8-9.5)

- Birth Cohort Testing was 4X more Effective in identifying HCV+ Patients
- Different approaches to BCT are all effective

Goals of HCV Therapy

● Sustained Virologic Response
  
  – SVR
  
  – “Cure”
  
  – HCV-RNA undetectable at 12 (SVR12) or 24 (SVR24) weeks after therapy is completed
  
  – Durable in > 99% of patients

**Effect of SVR on the Risk of Clinical Outcomes**

Meta-analysis of data on survival from 34,563 patients with HCV on the effect of SVR on the risk of liver transplant, HCC, death, and re-infection

**5-Year Risk of Death (All-Cause) by SVR**

<table>
<thead>
<tr>
<th></th>
<th>SVR</th>
<th>No SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>4.5</td>
<td>10.5</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>3.6</td>
<td>11.3</td>
</tr>
<tr>
<td>HCV/HIV Co-infected</td>
<td>1.3</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**5-Year Risk of HCC by SVR**

<table>
<thead>
<tr>
<th></th>
<th>SVR</th>
<th>No SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>2.9</td>
<td>9.3</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>5.3</td>
<td>13.9</td>
</tr>
<tr>
<td>HCV/HIV Co-infected</td>
<td>0.9</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**5-Year Risk of Liver Transplant by SVR**

<table>
<thead>
<tr>
<th></th>
<th>SVR</th>
<th>No SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>0.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>0.2</td>
<td>7.3</td>
</tr>
<tr>
<td>HCV/HIV Co-infected</td>
<td>0.6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

SVR was associated with:
- 62–84% reductions in all-cause mortality
- 90% reduction in need of transplantation
- 68–79% reductions in the risk of HCC

Chronic HCV Therapy (Genotype 1): Advances in Raising Cure Rates

SVR (%)

- 16% (1991)
- 35% (1998)
- 44% (2001)
- >70% (2011)

AE’s in 40+%:
- Depression
- Pancytopenia
- Rash
- Cough
- Flu-like sx’s
- Etc.
- Etc.
- Etc.
- Etc.

Chronic HCV Infection: Targets for Direct-Acting Antiviral Agents

- Prevent viral entry
  - Polyclonal and monoclonal antibodies

- Prevent translation of viral RNA
  - NS3/4 protease inhibitors

- Inhibit HCV-RNA polymerase
  - Nucleoside analogue NS5B polymerase inhibitors
  - Non-nucleoside analogue NS5B polymerase inhibitors
  - Replication complex inhibitor
  - Cyclophilin B inhibitors

- Viral assembly/release
  - Glucosidase inhibitor
<table>
<thead>
<tr>
<th>FDA Approval</th>
<th>NS3/4A Protease Inhibitor</th>
<th>Nucleotide NS5B Polymerase Inhibitor</th>
<th>Non-Nucleoside NS5B Polymerase Inhibitor</th>
<th>NS5A Replication Complex Inhibitor</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
<td>PegIFN ± RBV</td>
</tr>
<tr>
<td>2014</td>
<td>Sofosbuvir</td>
<td></td>
<td>Ledipasvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>Simeprevir</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>Paritaprevir</td>
<td>Dasabuvir</td>
<td>Ombitasvir</td>
<td></td>
<td>+ RBV</td>
</tr>
</tbody>
</table>
A Logical Approach to HCV Therapy

• 3 FDA-approved G1 DAA regimens
  – Cure rates are generally $> 90\%$

• AASLD-IDSA guidelines

• Prioritization
  – Staging of liver disease
    • 4 (cirrhosis) $> 3 > 2 > 1 > 0$ (no scar tissue)
  – Exceptions to staging
    • Cryoglobulinemia
    • Disease co-factors
“An assessment of the degree of hepatic fibrosis, using noninvasive testing or liver biopsy, is recommended.”

- HCV therapy prioritization

- Cirrhosis
  - Varices
  - HCC risk

- Class I, level A

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
Non-Invasive Staging Modalities

- Serologic markers and panels
  - FibroSURE, FibroSPECT, APRI, etc

- Transient elastography (FibroScan)

Non-invasive tests have been shown to:
- Determine stage of fibrosis
- Follow progression/regression of fibrosis
- Predict liver-related complications
- Predict survival
### AASLD/IDSA Guidelines: HCV Treatment Prioritization

#### Highest Priority for Treatment

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced fibrosis (Metavir F3)</td>
</tr>
<tr>
<td>Compensated cirrhosis (Metavir F4)</td>
</tr>
<tr>
<td>Organ transplant</td>
</tr>
<tr>
<td>Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations</td>
</tr>
<tr>
<td>Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis</td>
</tr>
</tbody>
</table>

#### High Priority for Treatment

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis (Metavir F2)</td>
</tr>
<tr>
<td>HIV or HBV coinfection</td>
</tr>
<tr>
<td>Other co-existent liver disease</td>
</tr>
<tr>
<td>Debilitating fatigue</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus (insulin resistant)</td>
</tr>
<tr>
<td>Porphyria cutanea tarda</td>
</tr>
</tbody>
</table>

AASLD and IDSA. Available at: [http://www.hcvguidelines.org/full-report-view](http://www.hcvguidelines.org/full-report-view)
CHeCS: Chronic Hepatitis Cohort Study: Prioritizing Patients for HCV Treatment

Observational database study evaluating priority per AASLD/IDSA guidance

Patients Staged by Biopsy or FIB-4 Score

- > F3: 30.0%
- < F3 with CKD: 2.9%
- F2: 22.7%
- < F2 with HIV/HCV: 4.9%
- < F2 with HBV/HCV: 0.4%
- < F2 with NASH: 0.7%
- < F2 with Diabetes: 0.2%
- Not meeting "highest or high" priority criteria: 38.2%

Xu et al. AASLD 2014, Abstract # LB29.
Implications of Cirrhosis

Hepatocellular carcinoma

“But you said I was cured of my hepatitis C!!!”
AASLD – IDSA HCV Guidelines (hcvguidelines.org)

- Expert panel

- HCV Guidelines based on:
  - FDA recommendations
  - Manufacturer’s recommendations
  - Literature
  - Expert opinion

- Recommendations:
  - Preferred
  - Alternative
  - Not recommended

- These do **NOT** necessarily follow the FDA recommendations!!!
Preferred Treatment Recommendations:

Naïve to Therapy

AASLD-IDSA + Package inserts

Genotype 1

- Sofosbuvir + Ledipasvir 8 weeks (no cirrhosis, RNA < 6m)
- Sofosbuvir + Ledipasvir 12 weeks

- Simeprevir + Sofosbuvir 12 weeks (without cirrhosis)
- Simeprevir + Sofosbuvir 24 weeks (with cirrhosis)

- 3D 12 weeks (1b without cirrhosis)
- 3D + RBV 12 weeks (1a without cirrhosis, 1b with cirrhosis)
- 3D + RBV 24 weeks (1a with cirrhosis)

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
Preferred Treatment Recommendations: Experienced Patients
AASLD-IDSA + Package inserts

Genotype 1

- Sofosbuvir + Ledipasvir 12 weeks (without cirrhosis)
- Sofosbuvir + Ledipasvir 24 weeks (with cirrhosis)
- Sofosbuvir + Ledipasvir + RBV 12 weeks (with cirrhosis)
- Simeprevir + Sofosbuvir 12 weeks (without cirrhosis)
- Simeprevir + Sofosbuvir 24 weeks (with cirrhosis)
- 3D 12 weeks (1b without cirrhosis)
- 3D + RBV 12 weeks (1a without cirrhosis, 1b with cirrhosis)
- 3D + RBV 24 weeks (with cirrhosis)

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
ION-1: SVR12 Rates With Sofosbuvir/Ledipasvir + RBV in Treatment-Naïve, HCV Genotype 1

12-Week Arm

<table>
<thead>
<tr>
<th></th>
<th>No RBV (n=214/179/33)</th>
<th>RBV (n=217/178/33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>99%</td>
<td>100%</td>
</tr>
<tr>
<td>No cirrhosis</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>97%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**SAPPHIRE-I: Ombitasvir/Paritaprevir/r + Dasabuvir + RBV in Treatment-Naïve, HCV Genotype 1**

### Phase 3
- Double-blind
- Genotype 1
- Treatment-naïve
- Non-cirrhotic
- 18 to 70 years of age

<table>
<thead>
<tr>
<th>Week</th>
<th>Ombitasvir/Paritaprevir/r + Dasabuvir + RBV (n=473)</th>
<th>Placebo (n=158)</th>
<th>Ombitasvir/Paritaprevir/r + Dasabuvir + RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Ombitasvir/paritaprevir/r 25/150/100 mg qd + dasabuvir 250 mg bid. RBV (1000-1200 mg).**

**Primary endpoint:** SVR12 versus historical control SVR rate: 78% (telaprevir + pegIFN + RBV).

**Baseline demographics and disease characteristics:**
- Male: 46% to 57%.
- Age: 52 years.
- Black: 5%-6%.
- Genotype 1a: 67%-68%.
- IL28B non-CC: 68%-70%.
- HCV RNA (log_{10} IU/mL): 6.5-6.6.
- Fibrosis stage F0-F1: 77%.

SVR12 rates were similar across patient subgroups

- Baseline HCV RNA, IL28B, BMI, fibrosis stage, gender, race

**SVR12 Rates**

<table>
<thead>
<tr>
<th>HCV Subtype</th>
<th>Overall (n=473)</th>
<th>1a (n=322)</th>
<th>1b (n=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>96%</td>
<td>95%</td>
<td>98%</td>
</tr>
</tbody>
</table>

*SAPPHIRE-I: Ombitasvir/Paritaprevir/r + Dasabuvir + RBV in Treatment-Naïve, HCV Genotype 1*

ION-2: SVR12 Rates With Sofosbuvir/Ledipasvir + RBV in Treatment-Experience, HCV Genotype 1

12-Week Arm

- No RBV (n=87/22)
  - No cirrhosis: 95%
  - Cirrhosis: 86%
- RBV (n=89/22)
  - No cirrhosis: 100%
  - Cirrhosis: 82%

24-Week Arm

- No RBV (n=87/22)
  - No cirrhosis: 99%
  - Cirrhosis: 100%
- RBV (n=89/22)
  - No cirrhosis: 99%
  - Cirrhosis: 100%

PR: pegIFN + RBV.

<table>
<thead>
<tr>
<th>Phase 2a</th>
<th>Non-cirrhotic (F0-F2)</th>
<th>Cirrhotic (F3-F4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open-label Genotype 1 Prior PR null responder</td>
<td>Simeprevir + Sofosbuvir qd (n=14)</td>
<td>Simeprevir + Sofosbuvir qd (n=14)</td>
</tr>
<tr>
<td></td>
<td>Simeprevir + Sofosbuvir qd + RBV (n=27)</td>
<td>Simeprevir + Sofosbuvir qd + RBV (n=27)</td>
</tr>
<tr>
<td></td>
<td>Simeprevir + Sofosbuvir qd (n=15)</td>
<td>Simeprevir + Sofosbuvir qd (n=16)</td>
</tr>
<tr>
<td></td>
<td>Simeprevir + Sofosbuvir qd + RBV (n=24)</td>
<td>Simeprevir + Sofosbuvir qd + RBV (n=30)</td>
</tr>
</tbody>
</table>

| Week | 0 | 12 | 24 |

COSMOS Subgroup Analysis: SVR12 in HCV Genotype 1, METAVIR F3-F4

SVR12

<table>
<thead>
<tr>
<th></th>
<th>12 Weeks (n=14/27)</th>
<th>24 Weeks (n=16/30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simeprevir + sofosbuvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No RBV</td>
<td>93%</td>
<td>100%</td>
</tr>
<tr>
<td>With RBV</td>
<td>93%</td>
<td>93%</td>
</tr>
</tbody>
</table>

## Preferred Treatment Recommendations: Naïve to Therapy

**AASLD-IDSA + Package inserts**

| Genotype 2 | Sofosbuvir + RBV 12 weeks  
|           | Sofosbuvir + RBV 16 weeks (cirrhosis) |
| Genotype 3 | Sofosbuvir + RBV 24 weeks  
|           | Sofosbuvir + PEG-IFN + RBV 12 weeks (alternative) |

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
## Preferred Treatment Recommendations: Experienced Patients

AASLD-IDSA + Package inserts

<table>
<thead>
<tr>
<th>Genotype 2</th>
<th>Sofosbuvir + RBV 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sofosbuvir + RBV 16 weeks (cirrhosis)</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir + PEG-IFN + RBV 12 weeks (alternative)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotype 3</th>
<th>Sofosbuvir + RBV 24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sofosbuvir + PEG-IFN + RBV 12 weeks (alternative)</td>
</tr>
</tbody>
</table>

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
VALENCE Trial: Sofosbuvir + RBV in HCV Genotypes 2 and 3

Phase 3 (Europe)
Open-label
Genotype 2 or 3
HCV treatment-naïve and experienced
Cirrhosis allowed

Genotype 2 or 3
Sofosbuvir qd + RBV (n=73/11)

Genotype 3 (amended protocol)
Sofosbuvir qd + RBV (n=250)

Baseline demographics and disease characteristics:
- Male: 55% to 62%
- IL28B non-CC: 64% to 74%
- HCV RNA (log_{10} IU/mL): 6.2-6.5
- Cirrhosis: 14% to 23%
- Prior pegIFN + RBV nonresponder: 24% to 44%
- Prior pegIFN + RBV relapser: 56% to 68%

VALENCE Trial: Sofosbuvir + RBV in HCV Genotype 2

VALENCE Trial: Sofosbuvir + RBV in HCV Genotype 3

Preferred Treatment Recommendations:
Naïve to Therapy
AASLD-IDSA + Package inserts

- Genotype 4
  - Sofosbuvir + Ledipasvir 12 weeks
  - Sofosbuvir + RBV 24 weeks
  - 3D + RBV 12 weeks

- Genotype 5
  - Sofosbuvir + PEG-IFN + RBV 12 weeks

- Genotype 6
  - Sofosbuvir + Ledipasvir 12 weeks

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
Preferred Treatment Recommendations: Experienced Patients
AASLD-IDSA + Package inserts

Genotype 4
- Sofosbuvir + Ledipasvir 12 weeks
- Sofosbuvir + RBV 24 weeks
- Sofosbuvir + PEG-IFN + RBV 12 weeks
- 3D + RBV 12 weeks

Genotype 5
- Sofosbuvir + PEG-IFN + RBV 12 weeks

Genotype 6
- Sofosbuvir + Ledipasvir 12 weeks
- Sofosbuvir + PEG-IFN + RBV 12 weeks (alternative)

AASLD and IDSA. Available at: http://www.hcvguidelines.org/full-report-view.
<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>LDV/SOF 12 and 24 Wk n=251</th>
<th>LDV/SOF + RBV 12 and 24 Wk n=262</th>
<th>TOTAL N=513</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>190 (76)</td>
<td>225 (86)</td>
<td>415 (81)</td>
</tr>
<tr>
<td>Treatment-related AE</td>
<td>118 (47)</td>
<td>196 (75)</td>
<td>314 (61)</td>
</tr>
<tr>
<td>Grade ≥ 3 AE</td>
<td>19 (8)</td>
<td>20 (8)</td>
<td>39 (8)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>15 (6)</td>
<td>9 (3)</td>
<td>24 (5)</td>
</tr>
<tr>
<td>Treatment-related serious AE</td>
<td>1 (&lt;1)</td>
<td>4 (2)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>AE leading to study drug modification/interruption</td>
<td>3 (1)</td>
<td>38 (15)</td>
<td>41 (8)</td>
</tr>
<tr>
<td>Treatment D/C due to AE</td>
<td>0</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Grade 3–4 lab abnormality</td>
<td>39 (16)</td>
<td>35 (13)</td>
<td>74 (14)</td>
</tr>
<tr>
<td>Hemoglobin &lt; 10 g/dL</td>
<td>1 (&lt;1)</td>
<td>26 (10)</td>
<td>27 (5)</td>
</tr>
<tr>
<td>Hemoglobin &lt; 8.5 g/dL</td>
<td>0</td>
<td>3 (1)</td>
<td>3 (&lt;1)</td>
</tr>
</tbody>
</table>

Bourliere et al. AASLD 2014, Abstract # 82.
SAPPHIRE-I: Safety of Ombitasvir/Paritaprevir/r + Dasabuvir + RBV in Treatment-Naïve, HCV Genotype 1

• Most common adverse events
  Nausea, pruritus, insomnia, diarrhea, asthenia

• Only 2 SAE’s possibly related to ombitasvir/paritaprevir/r + dasabuvir + RBV

<table>
<thead>
<tr>
<th>Adverse events (%)</th>
<th>3D + RBV (n=473)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3/4</td>
<td>2.1</td>
</tr>
<tr>
<td>Discontinuations</td>
<td>0.6</td>
</tr>
<tr>
<td>Death (number)</td>
<td>0</td>
</tr>
<tr>
<td>Laboratory abnormalities (%)</td>
<td></td>
</tr>
<tr>
<td>ALT &gt;5x ULN</td>
<td>0.9</td>
</tr>
<tr>
<td>AST &gt;5x ULN</td>
<td>0.6</td>
</tr>
<tr>
<td>Alkaline phosphatase &gt;5x ULN</td>
<td>0</td>
</tr>
<tr>
<td>Total bilirubin &gt;3x ULN</td>
<td>2.8</td>
</tr>
<tr>
<td>Hemoglobin &lt;10-8.0 g/dL</td>
<td>5.8</td>
</tr>
<tr>
<td>&lt;8.0 g/dL</td>
<td>0</td>
</tr>
</tbody>
</table>

Drug-Drug Interactions

- http://www.hep-druginteractions.org
A Logical Approach to HCV Therapy (cont.)

- Sim/Sof
- Sof + Ledipasvir
- 3D
- Sim/Sof + RBV
- Sof + Ledipasvir + RBV
- 3D + RBV
- Sof + PEG-IFN + RBV
- Sof + RBV
- Upcoming therapies
  - 8 weeks
  - 12 weeks
  - 16 weeks
  - 24 weeks
- Cirrhosis
- No cirrhosis
- Naïve
- Experienced
- Biopsy
- No biopsy
- FibroSURE
- FibroSCAN
- FibroTEST

$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$
A Logical Approach to HCV Therapy (cont.)

• Efficacy
  – Well-established

• Drug-drug interactions
  – Get used to them
  – All DAA’s have them

• Side effects
  – Well-tolerated and safe

• Cost
A Logical Approach to HCV Therapy (cont.): Cost

• Cost drives most (or all) HCV treatment decisions

• Insurance rules will vary
  – Who can be treated
  – What they can be treated with
  – How long they can be treated for

• Utilize additional resources
  – Specialty pharmacies
  – High-volume treaters
  – Pharmaceutical companies
    • Co-payment programs, etc
(print name) agrees to the following:

I have not abused alcohol, injectable drugs or other controlled substances for at least 6 months prior to starting Hepatitis C treatment, and I will not use these substances while being treated for Hepatitis C. If I am involved in a support group or counseling for addiction, I will continue therapy to encourage successful abstinence.

I have been reasonably adherent with all my current medications for all conditions and will take my Hepatitis C treatment daily as prescribed.

I have a history of showing up for scheduled appointments and labs and will continue to show up for all appointments and lab tests while taking Hepatitis C treatment.

If I have mental health conditions, I have been and will continue to adhere to my prescribed mental health medications and/or psychotherapy.

Patient signature: .................................................  Date: .................................................
Conclusions

- Birth-cohort screening for Hepatitis C (1945-1965)
  - Screening for HCV is currently suboptimal

- Cure of HCV (SVR) is highly beneficial

- Current treatments are very effective and safe
  - Naïve and experienced patients can be cured with DAA’s
  - An active pipeline for new and innovative therapies exists
  - Current and new regimens will be further optimized
    - ? Shorter duration
  - IFN and ribavirin are on life-support, but still hanging on
Conclusions (cont.)

- hcvguidelines.org for AASLD/IDSA revised guidelines

- Further study is needed for DAA’s in special patient populations
  - Advanced cirrhosis
  - HIV co-infection
  - Liver transplant recipients
  - Renal failure patients
  - Genotype 3, experienced, cirrhotics

- There will need to be a focus on access to care and cost
Chronic HCV Therapy (Genotype 1): Advances in Raising Cure Rates

SVR (%)

- 16% (1991)
- 35% (1998)
- 44% (2001)
- >70% (2011)

Telaprevir or Boceprevir + PegIFN/RBV

>90% (>2013)

2nd Generation DAAs PegIFN-Free Regimens

Questions