Expensive but Effective All Oral Chronic Hepatitis C Treatments—Update, and How to Improve Patient Access

Thomas E. Werth
University of Rochester Medical Center
Division of Gastroenterology and Hepatology

Acknowledgements

- Clinical Care Options (CCO)  [www.clinicaloptions.com/hepatitis](http://www.clinicaloptions.com/hepatitis)
- American Association for the Study of Liver Diseases (AASLD) and Liver Learning
- hcvguidelines.org  [www.hcvguidelines.org](http://www.hcvguidelines.org)

Hepatitis C virus

Single-stranded RNA virus

Spread through exposure to blood

Acute infection rarely accompanied by symptoms—immune response is Suboptimal

There are at least six subtypes, or "Genotypes" (GT)
Hepatitis C Virus Infection

Magnitude of the Problem

- Nearly 3 million persons in United States infected
- Estimated 140-170 million persons with HCV worldwide
- Approximately 35,000 new cases yearly
- About 12,000 deaths annually
- 85% of new cases become chronic
- Leading cause of:
  - Chronic liver disease, cirrhosis, liver cancer, liver transplantation

Hepatitis C Virus Infection
Population at Risk

- Transfusion of blood products before 1992
- Intravenous drug use*
- Nasal inhalation of cocaine
- Chronic renal failure on dialysis
- Incarceration
- Occupational exposure to blood products
- Transplantation of an organ/tissue graft from an HCV-positive donor
- Body piercing and potentially tattoo
- Those born between 1945-1965


Hepatitis C Virus
Genotypes in the USA

- Type 1: 72%
- Type 2: 17%
- Type 3: 10%
- All others: 1%


Role of Frontline Providers in HCV Screening

- Assess all patients for risk factors
- Offer testing to patients at risk and anyone who requests testing
- Guidelines: test all baby boomers, even those with normal ALT and no reported risk factors
Role of Frontline Providers in HCV Screening

- Assess all patients for risk factors
- Offer testing to patients at risk and anyone who requests testing
- Guidelines: test all baby boomers, even those with normal ALT and no reported risk factors
- If your patient tests positive for HCV antibody, please check HCV RNA Quantitative/Genotype

Chronic Hepatitis C Virus Extrahepatic Manifestations

- Nonspecific antibodies
- Essential mixed cryoglobulinemia
- Glomerulonephritis
- Porphyria cutanea tarda
- Leukocytoclastic vasculitis
- Non-Hodgkin’s lymphoma
- Autoimmune thyroiditis
- Diabetes mellitus
- Sjögren’s syndrome

HCV TREATMENT
I disclose the following financial relationship with a commercial interest: None.

HCV treatment historical timeline

And In 2013: Interferon Free

HCV Life Cycle

The virus appears to inhibit viral host defense mechanisms, including decreasing the production of interferons within the hepatocyte.
HCV Treatment Option: Interferon alpha, Effects

- Binds to Cell
- Stimulates interferon alpha and beta genes to induce antiviral state

HCV Treatment: Ribavirin

- Binds to Ribavirin
- Inhibits viral RNA synthesis
Definitions of Response to Treatment in HCV

SVR = Long term treatment success “Cure”

Sustained Virologic Response SVR = Eradication

Does SVR matter?

Eradication of Hepatitis C in Patients with Advanced Fibrosis and Cirrhosis

Eradication is associated with significantly lower rates of liver related death

SVR = sustained virologic response to treatment (Eradication)
Eradication of Hepatitis C Improves All-Cause Mortality Rates and Liver Complications

PEG Interferon/RBV response rates

- For Genotype 1 patients, overall response rates after months of treatment were about 40% chance of SVR (23% for African Americans)
- For Genotype 2/3, SVR rates up to 75%
**Interferon and Ribavirin Side Effects**
- Fatigue
- Flu-like symptoms
- Anorexia, weight loss
- Skin conditions
- Dry mouth
- Hair loss
- Neuropsychiatric conditions
- Anemia, leukopenia, neutropenia, thrombocytopenia

*High side effects, long treatment duration, Suboptimal efficacy...*

**Direct Acting Agents (DAA) in HCV**
- Protease Inhibitors (PI): NS3/4A inhibitors
- Nucleoside polymerase inhibitors (NPI): NS5B inhibitors
- Non Nucleoside polymerase inhibitors (NNPI): NS5B inhibitors
- Assembly and replication enzyme inhibitors: NS5A inhibitors

**HCV Life Cycle and Direct Acting Agent (DAA) Targets**
Targets for Treatment of HCV

2011: Protease Inhibitors (PI)
Triple therapy: PEG-IFN+ribavirin+PI

- **Telaprevir** (Incivek) (750 mg given every eight hours)
  - 1st 12 weeks of therapy
- **Boceprevir** (Victrelis) (800 mg given every eight hours)
  - 4 week PEG-IFN+ribavirin lead-in
- Duration of treatment: 24 weeks - 48 weeks

Telaprevir/P/R or Boceprevir/P/R produce a superior SVR to PEG-Interferon/Ribavirin (P/R) alone in treatment naive patients (Genotype 1)
Observational Study at Academic and Community Sites with Triple Therapy Are NOT as impressive

• SVR, Treatment Naive, GT1, Boceprevir: 58%
• SVR, Treatment Naive, GT1, Telaprevir: 61%

Dillsceglie AM et al. The Liver Meeting 2013 Abstract 41

Triple Therapy with Protease Inhibitor--Side Effects

• Fatigue
• Flu-like symptoms
• Anorexia, weight loss
• Skin conditions
• Dry mouth
• Hair loss
• Neuropsychiatric conditions
• Anemia, leukopenia, neutropenia, thrombocytopenia
• And in patients with Cirrhosis, Infection rates up to 10%, and death in up to 2%

The percentage of Hepatitis C patients treated by 2011 is very small...

![Graph showing percentage of Hepatitis C patients treated by 2011]
In 2013, Simeprevir approved as a second generation protease inhibitor as part of “triple therapy”: 12 weeks of Simeprevir with 24 weeks of PegIFN/RBV in GT1 HCV—SVR rates approach consistent 80%.

In 2013, a truly “breakthrough” drug for hepatitis C is approved for treatment.

Targets for Treatment of HCV
**Sofosbuvir, Nucleotide NS5B polymerase inhibitor**

- Potent, once daily drug
- Pan-genotypic effectiveness
- Few drug-drug interactions
- Few side effects
- Rare resistance problems
- Approved for GT1, GT4 as part of triple therapy: SOF + PegIFN + RBV for 12 weeks only

**NEUTRINO: Sofosbuvir + P/R for 12 Weeks in Treatment-Naive GT 1/4/5/6 HCV**

- Open-label, single-arm study of sofosbuvir 400 mg QD + P/R for 12 weeks in treatment-naive patients with GT1/4/5/6 HCV
  - 17% cirrhosis; 89% GT1; 9% GT4; < 1% GT5; 2% GT6

![Graph showing SVR12 rates for different genotypes and cirrhosis status.](image)

**Summary of Sofosbuvir + Peg IFN/R in GT1 HCV (2013)**

- **Pros**
  - Once-daily nucleotide polymerase inhibitor
  - Very well tolerated
  - Simple: given for only 12 weeks in all GT1 patients (no response guided therapy)
  - SVR >90% in noncirrhotics, and in cirrhosis 80%
  - Same regimen approved for GT4
- **Con**
  - Still uses high side effect drug Peg IFN
The Good News (For Genotype 1)

The Good News 90% is the new black

The Bad News: Contraindications to treatment with Interferon based therapy in HCV
- Uncontrolled depressive illness, psychosis, or epilepsy
- Untreated anemia (hemoglobin < 12 g/dL)
- Renal, heart, or lung transplantation
- Autoimmune hepatitis or other autoimmune condition known to be exacerbated by pegIFN and RBV
- Untreated thyroid disease
- Pregnancy or unwillingness to comply with adequate contraception
- Severe concurrent medical disease
- Known hypersensitivity

What about GT2 and GT3, and Sofosbuvir?

For most patients, the New Era began in 2014...

Interferon Free!

Sofosbuvir + RBV in HCV GT 2/3
Genotype 2 = 3
(No Interferon!)

A very effective regimen for nearly all GT2 patients
A very effective regimen for many GT3 patients
A very effective regimen for naïve GT3 pts

FAIRLY EFFECTIVE IN NON-CIRRHOTIC TREATMENT EXP GT3 PTS

Genotype 2 and 3 Approaches (2014)

- Genotype 2
  - SOF + RBV for 12 weeks for all populations
  - 93-100% SVR
- Genotype 3
  - Naïve (all populations)
    - SOF + RBV for 24 weeks (>90% SVR)
    - DAA combinations in future for 12 weeks
  - Treatment experienced
    - Non-cirrhotics: SOF + RBV 24 weeks (85% SVR)
    - Cirrhosis
      - SOF + RBV for 24 weeks (60% SVR)
      - PEG-IFN + RBV + SOF for 12 weeks (83% SVR)

New Standard of Care for HCV in 2013/2014

- Interferon + Ribavirin
- Peginterferon + Ribavirin
- Boceprevir or Telaprevir + P/R
- Sofosbuvir or Sofosbuvir + P/R

Standard Interferon


GT1 2011

GT2/3 2013

Sofosbuvir + Ribavirin

SVR 12 (%, G2/G3)

Nonnaïve Nonnaïve Naïve Naïve Treatment-experienced

SVR 12 = 83%
Hepatitis C: 2014 into 2015

• Many patients are as yet undiagnosed
• The vast majority of patients have not been treated, and many that were did not achieve SVR
• The side effects of treatment, cost and contraindications to treatment are all a significant barrier to care
• Are there treatments, now or in the future, that may be better, and if so, in what way?

Hepatitis C 2015

If you treat hepatitis C patients for a long enough period of time, with effective therapy, you will eradicate the virus in nearly every patient who is compliant with therapy.

Targets for Treatment of HCV
**Direct Acting Agents (DAA) in HCV**

- Protease Inhibitors (PI): NS3/4A inhibitors
- Nucleoside polymerase inhibitors (NPI): NS5B inhibitors
- Non Nucleoside polymerase inhibitors (NNPI): NS5B inhibitors
- Assembly and replication enzyme inhibitors: NS5A inhibitors

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**HCV Life Cycle and DAA Targets**

- Receptor binding and endocytosis
- Fusion and uncoating
- Transport and release
- (+) RNA translation and polyprotein processing
- RNA replication
- Virion assembly
- Membranous web
- ER lumen
- LD

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**Multiple Direct Acting Antivirals**

- Protease
  - HCV PI
    - Telaprevir
    - Boceprevir
    - Tipranavir
    - Aliquoprevir
    - ABT-450
    - MK-712
    - Suvorexant
    - ACH-3184

- NS5A inhibitors
  - NS5A inhibitors
    - Dalaprevir
    - Ledipasvir
    - ABT-267
    - GS-5816
    - ACH-3192
    - PP-68
    - GS-8430805
    - Sofosbuvir
    - VX-157
    - IDX29653
    - ACH-3422

- NS5B inhibitors
  - NS5B inhibitors
    - Sofosbuvir
    - VX-157
    - IDX29653
    - ACH-3422

- NS5B non-nucleoside
  - NS5B non-nucleoside
    - ABT-331
    - De Beaucourt
    - SM-721875
    - PP-385
    - GS-5816
    - TMCS4/3565
Why are there so many DAA's?!

A. It has been discovered that combinations of DAA's leads to high SVR, w/o interferon, in just 12 weeks of treatment
B. There is a need—huge numbers of HCV patients are yet to be treated, or failed treatment.
C. Potential for high return on investment for pharmaceutical companies based on low production costs/number of patients.
D. Negotiating a price for a drug treatment for a particular combination of effective DAA's may be easier if all the DAA's in that combination are manufactured/marketed by the same company.
E. All of the above

Multiple Direct Acting Antivirals

IFN-Free Therapies: Considerations
Especially Focusing on GT1

- How many DAAs?
- Which combinations?
- One size fits all vs tailored therapy, especially for GT1a (more resistance seen) vs GT1b?
All oral DAA Options GT1

- PI backbone—potent/modest barrier to resistance
  - PI + 1 low-barrier DAA (NNI/NS5A)
  - PI + 2 low-barrier DAA
- Nucleoside NS5B backbone – potent/high barrier
  - Nuc NS5B + low-barrier DAA = NS5A
  - Nuc NS5B + PI
- Include ribavirin?
  - May allow fewer DAA (2 vs 3)
  - May allow shorter therapy

Multiple Direct Acting Antivirals
Nuc NS5B Backbone + NS5A

- SOF (Nuc) + daclatasvir (NS5A) ± RBV x 24 wks
- SOF (Nuc) + daclatasvir (NS5A) ± RBV x 12 wks

Major caveats: small n, no plan for phase III trial


Virologic Response during and after Treatment.

Multiple Direct Acting Antivirals
1-Pill Version of NS5B (Nuc) + NS5A

- No breakthrough, 2 relapses, both without RBV
- 1 case of resistance – retreated with SOF/LDV + RBV x 24 weeks → SVR


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Abstract #739

EASL 2014

All Oral Fixed-Dose Combination Ledipasvir/Sofosbuvir With Or Without Ribavirin for 12 or 24 Weeks in Treatment-Naive Genotype 1 HCV-Infected Patients: the Phase 3ION-1 Study

Alessandra Mangia, 1 Patrick Marcellin, 2 Paul Kuo, 3 Graham B. Felices, 1 Maria Bubu, 1 Herbert Brink, 1 Andrea Mutti, 1 Jenny C. Liang, 1 Hongmen Ishii, 1 Xiaoting Li, 1 Phil S. Pang, 1 William T. Symonds, 1 John S. McHutchison, 4 Stefan Zuzak, 5 Reem Aishah Al-Mahall4

1 Casa Sollievo della Sofferenza Hospital, San Giovanni Ribatorti, Italy; 2 Centre Hospitalier Universitaire Bruxon, Clichy-sous-Bic, France; 3 Indiana University School of Medicine, Indianapolis, IN, USA; 4 Queen Mary’s University of London, Barts Health, UK; 5 Hospital Universitario Valle de Hebron, Barcelona, Catalonia, Spain; 6 Mount Sinai School of Medicine, New York, NY, USA; 7 Duke University Medical Center Durham, NC, USA; 8 Gilead Sciences, Inc., Foster City, CA; 9 Johannes Wolfgang Goethe-University, Frankfurt, Germany; 10 Beth Israel Deaconess Medical Center, Boston, MA, USA.

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Results: SVR12

GT 1 Treatment-Naive (ION-1)

Error bars represent 95% confidence intervals.
All oral DAA Options GT1

- PI backbone—potent/modest barrier to resistance
  - PI + 1 low-barrier DAA (NNI/NS5A)
  - PI + 2 low-barrier DAA
- Nucleoside NS5B backbone – potent/high barrier
  - Nuc NS5B + low-barrier DAA
  - Nuc NS5B + PI
- Include ribavirin?
  - May allow fewer DAA (2 vs 3)
  - May allow shorter therapy

Multiple Direct Acting Antivirals

Example of Nuc Backbone + PI in Trt-Naive Pts and Nulls (COSMOS)

- SMV (PI) + SOF (Nuc) + RBV 12 wks
- SMV (PI) + SOF (Nuc) 12 wks


Major caveats: small n, no plan for phase III trial
Nucleotide NS5B Backbone

**Sofosbuvir + NS5A**
- Highly effective at reaching the 90% threshold
- Sofosbuvir + Daclatasvir
- Sofosbuvir + Ledipasvir

**Sofosbuvir + Simeprevir (PI)**
- Numbers are small but promising for 90%

All oral DAA Options GT1

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  - Nuc NS5B + PI
- Include ribavirin?
  - May allow fewer DAA (2 vs 3)
  - May allow shorter therapy

Multiple Direct Acting Antivirals
These drugs also known as ombitasvir/paritaprevir/ritonavir/dasabuvir
All oral DAA Options GT1

- PI backbone—potent/modest barrier to resistance
  - PI + 1 low-barrier DAA (NNI/NS5A) for GT1b
  - PI + NS5A + NonNuc NS5B +/- RBV for GT1a and GT1b
- Nucleoside NS5B backbone – potent/high barrier
  - Nuc NS5B + NS5A for both GT1a/b
  - Nuc NS5B + PI limited data
- Include ribavirin?
  - In selected regimens without sofosbuvir, it may allow a one size fits all therapy, either to allow treatment of both GT1a and GT1b, or achieve 90% threshold in the previously treated nonresponder cirrhotic

TURQUOISE-II: Safety Overview

<table>
<thead>
<tr>
<th>Event, %</th>
<th>12-Week Arm (N=208)</th>
<th>24-Week Arm (N=172)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>91.8</td>
<td>90.7</td>
</tr>
<tr>
<td>Severe AE</td>
<td>6.7</td>
<td>7.6</td>
</tr>
<tr>
<td>Serious AE</td>
<td>6.3</td>
<td>4.7</td>
</tr>
<tr>
<td>AE Leading to Drug Discontinuation</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>Death*</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*1 patient with a non-treatment emergent death (occurring 80 days after last dose of study treatment), not attributed to 3D or RBV.

- Hepatic decompensation events were rare (4 patients, 1.1%)
  - None were considered related to study drug
DAA’s: Side effects/Drug-Drug Interactions

• Most common side effects in most studies: headache, nausea, fatigue
• Anemia with ribavirin is much less common than when it was used with interferon
• Few serious adverse events
• Drug-drug interactions much less of an issue than with first generation PI’s, but still need to be reviewed prior to treatment initiation

Direct Acting Agents for Hepatitis C: For Most patients to achieve SVR of > 90%

• For Genotype 1 patients, interferon is no longer being used
  Sofosbuvir + Ledipasvir or Daclatasvir for 12 weeks
  ABT450r/ABT333/ABT250*** + Ribavirin for 12 weeks
• For Genotype 2: Sofosbuvir + Ribavirin for 12 weeks
• For Genotype 3: Sofosbuvir + Ribavirin for 24 weeks, or with Interferon for 12 weeks
• HOWEVER, there are many variations in duration of therapy and use of Ribavirin based on: viral load, cirrhosis, subtype of Genotype 1, previous treatment failure, etc...

***Ombitasvir/Paritaprevir/ritonavir/Dasabuvir

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• www.hcvguidelines.org

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www.hcvguidelines.org
# AASLD/IDSA Guidance: Genotype 1 HCV Recommended Regimen Examples

<table>
<thead>
<tr>
<th>Population</th>
<th>LDV/SOF</th>
<th>OMV/PTV/RTV + DSV</th>
<th>SMV + SOF</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT 1a, no cirrhosis</td>
<td>12 wks</td>
<td>12 wks + RBV</td>
<td>12 wks ± RBV</td>
</tr>
<tr>
<td>GT 1b, no cirrhosis</td>
<td>12 wks</td>
<td>24 wks + RBV</td>
<td>24 wks ± RBV</td>
</tr>
<tr>
<td>GT 1b, cirrhosis</td>
<td>12 wks</td>
<td>24 wks + RBV</td>
<td>24 wks ± RBV</td>
</tr>
<tr>
<td>GT 1 P/R failure, no cirrhosis</td>
<td>12 wks</td>
<td>12 wks + RBV (1a)</td>
<td>12 wks ± RBV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 wks or 12 wks + RBV (1b)</td>
<td>24 wks ± RBV</td>
</tr>
<tr>
<td>GT 1 P/R failure, cirrhosis</td>
<td></td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>GT 1 SOF failure, no cirrhosis</td>
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AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C.

# Pooled Data: Impact of Tx Duration and RBV in Cirrhotic GT1 Pts (LDV/SOF)

- Pooled data: ONESTAR, ELECTRON, ELECTRON-2, 337-013, 337-015, DOV-2, SARLA
- No difference in SVR rate by HCV subtype

![Graph showing SVR12 results](image)


# COST
COST

Will be the BIGGEST Barrier to Care

Recently approved therapies for HCV infection and 1-time birth-cohort screening could prevent approximately 124,200 cases of decompensated cirrhosis, 78,800 cases of hepatocellular carcinoma, 126,500 liver-related deaths, and 9900 liver transplantations by 2050.

The ideal scenario could reduce the total number of cases of decompensated cirrhosis by 135,800 (46%), cases of HCC by 96,300 (40%), liver-related deaths by 161,500 (37%), and liver transplantations by 13,900 (37%) during 2014 to 2050.

“Pharma”

$1,125

The current WAC for Harvoni is set at $1,125 per pill, which translates to $63,000 for eight weeks of treatment, $94,500 for 12 weeks and $189,000 for 24 weeks. Oct 14, 2014

WAC = wholesale acquisition cost

“Pharma”

Sofosbuvir + Simeprevir, 12 weeks = Approx $168,000
Sofosbuvir, 12 weeks = $84,000
Sofosbuvir + Ledipasvir, 12 weeks = $95,000
Ombitasvir/Paritaprevir/ritonavir/Dasabuvir= $83,300

Wholesale acquisition cost
“PAYERS”

- With the exception of mandated rebates, negotiations of drug prices are considered confidential business contracts and, therefore, there is almost no transparency regarding the actual prices paid for hepatitis C drugs. However, the average negotiated discount is reported to be 46% off the WAC in 2015, implying that most payers are paying well below the WAC (wholesale acquisition cost) price for HCV regimens.

Saag M. Getting smart in how we pay for HCV drugs: KAOS vs CONTROL. Clin Inf Dis. 2015; 61. DOI: 10.1093/cid/civ221. And hcvguidelines.org

“PATIENTS”

Hepatitis C is a Disease of the Disenfranchised

- In 33 state Medicaid programs, patients must have a score of F3 or F4 (F4 Metavir score is equal to cirrhosis) to receive sofosbuvir. Four states require biopsy to check fibrosis levels. (Ann Intern Med. Published online June 29, 2015)

- Twenty-nine states have restrictions based on prescriber type, and in 14 of them, the prescriber has to be a specialist (gastroenterology, hepatology, infectious diseases, or liver transplantation); in the other 15, decisions can be made by a nonspecialist after consultation with a specialist. (Ann Intern Med. Published online June 29, 2015)

- Many private insurers also hold to similar practices

These provisions lack scientific foundation or medical justification. - hcvguidelines.org

“PAYERS”

Barrier to Care: Cost and Budgets

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These provisions lack scientific foundation or medical justification. - hcvguidelines.org
Who will get access to the New DAA therapy? hcvguidelines.org (AASLD, IDSA, IAS-USA) originally said...

- Patients with hepatitis C should be treated
- Certain patients should be prioritized: Patients with F2, F3, F4, extrahepatic manifestations, coinfection with HIV or HBV, NASH, severe fatigue, DM, PCT, active injection drug users, incarcerated persons, dialysis patients...

www.hcvguidelines.org

- "...it is therefore difficult to estimate the true cost and cost-effectiveness of HCV drugs. Whatever the actual current cost of HCV DAs, competition and negotiated pricing have not improved access to care for many persons with HCV infection and continue to limit the public health impact of these new therapies. Insurers, government, and pharmaceutical companies should work together to bring medication prices to the point where all of those in need of treatment are able to afford and readily access it."
- "Accordingly, the HCV Guidance does not utilize cost-effectiveness analysis to guide recommendations at this time."

Infectious Diseases Society of America (IDSA) and American Association for the Study of Liver Diseases (AASLD), in collaboration with the International Antiviral Society–USA (IAS–USA)

Who will get access to the New DAA therapy? hcvguidelines.org (AASLD, IDSA, IAS-USA)

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On October 22, 2015, the following appeared on the hcvguidelines.org website:
"the panel continues to recommend treatment for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Accordingly, prioritization tables are now less useful and have been removed from this section."
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<tr>
<td>• Advanced fibrosis (F3, F4-cirrhosis)</td>
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<tr>
<td>• Abstinence from alcohol and illicit drugs</td>
<td></td>
</tr>
<tr>
<td>• Mandatory drug and alcohol counseling</td>
<td></td>
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<tr>
<td>• No malignancy of any organ</td>
<td></td>
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<tr>
<td>• “Extensive experience” treating HCV patients</td>
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<td>• Onerous prior authorization processes</td>
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</tr>
<tr>
<td>• Advanced fibrosis (F3, F4-cirrhosis)</td>
<td></td>
</tr>
<tr>
<td>• Abstinence from alcohol and illicit drugs</td>
<td></td>
</tr>
<tr>
<td>• Mandatory drug and alcohol counseling</td>
<td></td>
</tr>
<tr>
<td>• No malignancy of any organ</td>
<td></td>
</tr>
<tr>
<td>• “Extensive experience” treating HCV patients</td>
<td></td>
</tr>
<tr>
<td>• Onerous prior authorization processes</td>
<td></td>
</tr>
</tbody>
</table>

These provisions lack scientific foundation or medical justification—hcvguidelines.org
Reaching those Affected with HCV
How can we provide better access to care?

- Collaboration, cross-training of providers on risk factors, screening, and treatment so as many patient as possible have a chance at Cure
- Outreach, substance abuse education and counseling to continue to work on prevention
- Advocacy so that our HCV patients do not get caught in a fight over drug cost, budgets and competing financial goals

Thank you!

Supplement slides follow...
Decompensation Shortens Survival


Assessing Cirrhosis Severity:
Child-Pugh Score

<table>
<thead>
<tr>
<th>Variable Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy grade</td>
<td>None</td>
<td>1-2</td>
<td>3-4</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td>Prothrombin time [sec prolonged]</td>
<td>&lt; 4</td>
<td>4-6</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>Serum bilirubin [mg/dL]</td>
<td>&lt; 2</td>
<td>2-3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>Serum bilirubin if cholestatic disease [mg/dL]</td>
<td>&lt; 4</td>
<td>4-10</td>
<td>&gt; 10</td>
</tr>
</tbody>
</table>

- Child-Pugh A: 5-6 points
- Child-Pugh B: 7-9 points
- Child-Pugh C: ≥ 10 points

Subjective component relies on clinical judgment

Assessing Cirrhosis Severity: Model for End-Stage Liver Disease (MELD) Score

MELD score = 0.957 \times \log_e(\text{creatinine mg/dL}) + 0.378 \times \log_e(\text{bilirubin mg/dL}) + 1.120 \times \log_e(\text{INR})

- Continuous measure of liver disease severity
- Derived from pts undergoing transjugular intrahepatic portosystemic shunt placement (TIPS)
- Based on objective parameters
- Accurate predictor of 3-mo mortality
- Independent of complications of portal hypertension
- Independent of etiology


Hepatitis C Pts With Cirrhosis

- Pts with well compensated disease (Childs A, MELD < 15) achieve similar SVR rates as those without cirrhosis
- SVR may prevent further decompensation
- Decompensation associated with reduced survival and reduced response to therapy
- Recognize clinical, laboratory, and radiological signs of decompensation
  - Childs A transition to Childs B
  - Rising MELD to > 15


Newer Combination DAA-Experienced Pts Will Appear in Your Practice

- Sofosbuvir + simeprevir
- Ledipasvir/sofosbuvir
- Ombitasvir/paritaprevir/ritonavir + dasabuvir
- Failure of newer DAA regimens generally presents as relapse with RAVs to at least 1 class
• Of 16 pts with relapse, 11 had cirrhosis
• 1 of 16 relapses occurred between posttreatment Wks 4 and 12


AASLD/IDSA Guidance for HIV/HCV Coinfection
• Same recommendations as in HCV-monoinfected patients, but consider drug–drug interactions
  – Need to adjust or withhold RTV if receiving a boosted PI with OMV/PTV/RTV + DSV
  – Potential for LDV-mediated increase in tenofovir levels, especially if tenofovir used with RTV
  – Avoid DSV if CrCl < 60 mL/min or if receiving tenofovir with RTV-boosted PI
  – OMV/PTV/RTV + DSV can be used with raltegravir (and probably dolutegravir), enfuvirtide, tenofovir, emtricitabine, lamivudine, atazanavir
  – SMV can be used with: raltegravir (and probably dolutegravir), rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, abacavir
• Other interactions at aidsinfo.nih.gov/guidelines, hiv-druginteractions.org

AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C.

BOSON: SOF + PegIFN/RBV for 12 Wks vs SOF + RBV for 16 or 24 Wks in GT2/3 HCV
• Multicenter, randomized, open-label study
  – Key baseline characteristics: 92% GT3, ~ 38% IL28B CC, ~ 53% previously treated, ~ 37% with cirrhosis

<table>
<thead>
<tr>
<th>Table: SVR12, % (n/N)</th>
<th>GT2</th>
<th>GT3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratifed by cirrhosis, HCV GT, previous HCV tx</td>
<td>87/15 (13/15)</td>
<td>71/181 (128/181)</td>
</tr>
<tr>
<td>Wk 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratifed by cirrhosis, HCV GT, previous HCV tx</td>
<td>100/17 (17/17)</td>
<td>84/182 (153/182)</td>
</tr>
<tr>
<td>Wk 24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratifed by cirrhosis, HCV GT, previous HCV tx</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

*RBV: 1000-1200 mg/day. †PegIFN alfa-2a: 180 μg/wk.

Foster GR, et al. EASL 2015. Abstract 105G.