Evolving Role of Current & Emerging Therapies in the Management of Hepatitis C (HCV)

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SUN CITY
Objectives

• Learn the current and future treatment strategies for HCV
• Understand the epidemiology and natural history of HCV
• Learn how to diagnose and screen for HCV
Hepatitis C Virus (HCV)

- Single-stranded RNA virus
- Only member of genus *Hepacivirus* in the Flaviviridae family
- Humans are the only known natural host
- Unlike the DNA viruses HIV and HBV, *CURE* of HCV infection is possible

Hepatitis C Differs from HIV and HBV: HCV can be Cured!

**HBV**
- Host cell
- cccDNA
- Host DNA
- Nucleus

**HIV**
- Proviral DNA

**HCV**
- Viral RNA

TREATMENT
- Long-term suppression of viral replication

**1.** Pawlotsky JM. *J Hepatol* 2006;44:S10-S13;
**2.** Siliciano JD, Siliciano RF. *J Antimicrob Chemother* 2004;54:6-9;
**3.** Lucas GM. *J Antimicrob Chemother* 2005;55:413-416
EPIDEMIOLOGY OF HCV

Chronic HCV: A Global Health Problem

Weekly Epidemiological Record. N° 49, 10 December 1999, WHO
**HCV Genotypes**

6 HCV genotypes that differ from each other by 31-34% in their nucleotide sequences

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**Genotype and Viral Load in U.S. Patients**

- **Genotype 1**
  - HVL: 49.5%
  - LVL: 24.5%

- **Genotype 2,3**
  - HVL: 14.7%
  - LVL: 7.3%

- **Genotype 4,5,6**
  - HVL: 2.7%
  - LVL: 1.3%

**Viral Load Classification**
- **HIGH VIRAL LOAD:** >800,000 IU/ML
- **LOW VIRAL LOAD:** <800,000 IU/ML

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Current Prevalence of HCV

- 200 million persons have been infected with HCV worldwide (anti-HCV positive)\(^1\)
- 170 million have chronic disease worldwide (HCV RNA positive)\(^1\)
- 3.5 million Americans have been infected with HCV (anti-HCV positive)\(^2\)
  - True prevalence at least 5.2 million\(^3\)
- 2.7 million Americans have chronic disease (HCV RNA positive)\(^2\)

1. Edlin BR. Hepatology 2005;42(suppl 1):213A.
3. Chak E, Talai AH, Sherman KE, Schiff ER, Saab S. Liver International 2011; 31:1090-1101

Chronic HCV Infection in the US

- Chronic HCV cases not included in NHANES estimate:
  - Homeless
  - Incarcerated
  - Veterans
  - Active military
  - Healthcare workers
  - Nursing home residents
  - Chronic hemodialysis
  - Hemophiliacs

Chak E, Talai AH, Sherman KE, Schiff ER, Saab S. Liver International 2011; 31:1090-1101
Prevalence of HCV in the U.S. (NHANES 2001-2010)

Overall prevalence: 1% (2.7 million), 81% were born between 1945 and 1965 (Baby Boomers)


Chronic HCV in U.S. (3.2M)

59% of diagnosed HCV patients UNTREATED ~590K (18% of all HCV)
41% of diagnosed HCV patients TREATED ~410K (13% of all HCV)

ALF @ www.liverfoundation.org/education/info/hepatitis. Accessed April 8, 2014
CDC Hepatitis C fact sheet. @ www.cdc.gov. Accessed April 8, 2014
Natural History of HCV: A Chronic Progressive Liver Disease

HCV Natural Disease Progression

- Virus Cleared
  - Anti-HCV (+)
  - HCV-RNA (-)
  - 15% - 25% (>6 months)

- Acute HCV
  - 75% - 85% (>6 months)

- Chronic HCV
  - Anti-HCV (+)
  - HCV-RNA (+)
  - 60% - 70%

- Fibrosis
  - 20-30% (20-30 years)

- Cirrhosis
  - 1% - 4% per year

- Hepatocellular Carcinoma (HCC)

**HCV Disease Progression**

- **Stage 0**: No Fibrosis
- **Stage 1**: Portal Fibrosis
- **Stage 2**: Periportal Fibrosis
- **Stage 3**: Bridging Fibrosis
- **Stage 4**: Cirrhosis


**Chronic HCV: Progression to Cirrhosis**

- Mild
- Moderate
- Severe
- Cirrhosis
- Decom. Cirrhosis
- HCC

15%-30% of patients
20%-30% of patients
50-65% of patients

Shiffman ML. Viral Hepatitis Rev. 1999;5:27-43
Factors Associated With Disease Progression

- ETOH consumption: >30 g/day in males
  >20 g/day in females
- Disease acquisition at > 40 years
- Male
- HIV or HBV co-infection
- Hepatic Steatosis: obesity, metabolic syndrome

Swain et al. EASL 2005.

Factors Associated With Disease Progression: ETOH

- > 30 g/day in male: 2-3 drinks
- > 20 g/day in females: 2 drinks

HCV and Alcohol

Excessive alcohol intake characterized as > 20 g/day for women and > 30 g/day for men

Factors Associated With Disease Progression: Age

Patients infected with HCV when over 40 have a higher degree of fibrosis regardless of how long they have had the disease

HCV Fibrosis Progression: Effect of Age

Factors Associated With Disease Progression: Obesity

Obesity-related insulin resistance can lead to fatty liver and NASH and accelerate the development of fibrosis in HCV


Fibrosis Progression in HCV: Effect of Hepatic Steatosis

![Graph showing fibrosis progression with different steatosis levels over months.]


Factors Not Influencing Progression

- Transaminase level (ALT)
- Viral load
- Mode of transmission
- Genotype

Swain et al. EASL 2005.
Chronic HCV: The Epidemic has Just Begun

At least 2.7 million persons are chronically infected with HCV

Between 2010-2030 if NO treatment is provided

1,040,000 will have developed cirrhosis
254,664 will have developed HCC
537,928 will die


Estimated Prevalence of Chronic HCV and Cirrhosis

- Acute infections peaked between 1970 and 1990
- The peak of chronic HCV prevalence was 2001
- The highest prevalence of cirrhosis is projected to be between 2010 and 2030

The Tsunami of HCV Cirrhosis Complications: Decompensation and HCC

Hepatic decompensation
- Ascites
- Variceal bleed
- Encephalopathy

Diagnosis & Screening of HCV

Importance of Diagnosing HCV

- The Primary Care Provider (PCP) has a unique window of opportunity to make a diagnosis of HCV and refer for treatment prior to the development of cirrhosis and its complications
  - Improved survival
  - Improve quality of life
  - Will reduce the economic burden of HCV and result in cost savings

HCV Screening Is the First Step on the Road to a Cure

- Screening
- Counseling
- Evaluation
- Treatment
- Cure
HCV Patients Are Undiagnosed Because of Screening Barriers to Diagnosis

- Patient Barriers
  - Persons infected with HCV are usually asymptomatic and unaware of their infection
  - Persons infected with HCV are usually unaware of the risk factors for HCV

I hope I don’t have Hepatitis C
The Lack of Symptoms in Chronic HCV Infection

The most common symptom is fatigue

HCV Patients Are Undiagnosed Because of Screening Barriers to Diagnosis

• Primary Care Provider Barriers
  – Routine HCV risk factor assessment not current PCP practice
  – Elevated LFTs, not risk factors, is current marker for PCPs ordering a liver panel

Common Risk Factors for HCV

HCV is spread through contact with infected blood

- IV drugs use now accounts for 2/3 of HCV in US
- Received blood or blood products or solid organ transplant before 1992
- Hemodialysis patients before 1992
- Needle Sticks

Common Risk Factors for HCV

HCV is spread through contact with infected blood

- Intranasal cocaine with shared implements
- Body piercing with contaminated needles
- Tattooing with contaminated needles or ink
- Incarceration
Less Common Risk Factors

• Sharing of household items that could carry infected blood: razors, toothbrushes, manicure implements
• Traumatic contact with blood: cuts, nosebleeds, menstrual blood
• Perinatal transmission: 5% of deliveries from HCV positive mothers


Less Common Risk Factors

• Sexual transmission: accounts for less than 5% of all cases: Seen in high-risk sexual behavior (multiple sex partners, prostitutes, man to man sex) where there is trauma to the mucosa)
  – The risk in monogamous partners is extremely low

The Role of the PCP: Look for Risk Factors

It’s been up to the PCP to identify and screen all their patients with risk factors for HCV.

Ask about Risk Factors when Asking about Alcohol and Tobacco
Risk-based Screening is not Working: You Can’t Treat What You Haven’t Diagnosed

Diagnosed HCV cases

Undiagnosed HCV cases

BABY BOOMERS

The CDC in 2012 and the US Preventive Services Task Force (USPSTF) in 2013 have recommended a 1-time screening for all persons born between 1945 and 1965 because of their high prevalence of HCV

- With Obamacare all screening tests recommended by the USPSTF will be free
Screening Guidelines for Diagnosing Chronic HCV

- Screen all baby boomers and all patients with risk factors regardless of age and all patients with ↑ LFT’s with EIA anti-HCV
  - >99% sensitivity
- In patients with ↑ LFT’s, look for other causes of ↑ LFT’s:
  - HAAb, HBsAg, HBcAb, HBsAb
  - Iron, TIBC, ferritin
  - Antinuclear, antimitochondrial, and antismooth muscle antibodies
Diagnosis of HCV

- Confirm positive anti-HCV with **quantitative** HCV RNA PCR
  - Positive within 1-3 weeks after exposure
  - Denotes active disease and infectivity
  - Quantitative assays detect to low levels: Quest Heptimax (5 IU/ml) or LabCorp Quanta-Sure (10 IU/ml)

- Check HCV genotype at the same time

Serologic Pattern of Chronic HCV

![Graph showing the serologic pattern of chronic HCV, including titers of anti-HCV, HCV RNA, and ALT over time after exposure.](image)
Goals of Treatment of HCV

- **Primary Goal:**
  - Permanent eradication of virus from serum: Sustained Viral Response (SVR)
    - Undetectable HCV RNA 6 months after completion of treatment with current treatment regimes
    - Undetectable HCV RNA 3 months after treatment with the newer combinations in the future
  - SVR is *synonymous* with “cure”
Sustained Virologic Response (SVR) Leads to Improved Outcome

SVR

- Viral Eradication
- Improved Clinical Outcomes
- Improved Liver Histology

↓ Decompensation
↓ HCC
↓ Mortality


Improvements in Therapy of HCV

<table>
<thead>
<tr>
<th>Year of publication</th>
<th>Phase 3 NEUTRINO: Lawitz E, et al. APASL 2013, Singapore, Oral #LB-02</th>
<th>SVR12 rate of 90% among GT 1 patients in the Phase 3 NEUTRINO trial (12 weeks of SOF+PEG-IFN+RBV)</th>
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<tbody>
<tr>
<td>INF</td>
<td>INF/RBV</td>
<td>PEG/INF/RBV 2001 DAA’s 2011 2nd Gen DAA’s 2013 INF Free</td>
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<td>INF 6 mo</td>
<td>INF 12 mo I/FN 6 mo I/FN/RBV 12 mo  PEG-IFN 12 mo  PEG-INF/RBV 12 mo  PI/PEG-INF/RBV 6-12 mo SMV + Peg-INF/RBV 6-12 mo SOF/PEG-INF/RBV 3 mo</td>
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<td>6</td>
<td>16 34 42 39 54-56 68-75 80-81 90 90+</td>
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Up to 2011, the Treatment of HCV GT1 was Pegylated Interferon and Ribavirin

- The unsatisfactory response rate in genotype 1 (54-56%) led to the development of a new class of HCV drugs called **Direct Acting Antivirals (DAA’s)** that directly inhibit viral replication.

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**HCV Life Cycle and DAA Targets**

HCV Genome and DAA Targets

Emergence of Pre-existing Resistant Mutants During Treatment with DAA Monotherapy
Use of Multiple Drugs Prevent Selection of Resistant Variants

All DAA’s now and in the future are used in combination with other HCV drugs to prevent viral resistance.

The First DAAs were 2 Protease Inhibitors: Telaprevir and Boceprevir with PegINF and Ribavirin

Limitations:

- They are only approved for genotype 1
- Efficacy: Many patients don’t achieve SVR
- Tolerability
- Complicated Regimens
- Serious drug-drug interactions

Higher discontinuation rates in real-world settings than in clinical trials
Second Generation DAA’S

• Goal:
  – Increase genotype 1 SVR
  – Shorten the duration of treatment
  – Avoid serious side effects
  – Improve SVR in genotypes other than 1
• The first FDA approved 2nd generation DAAs are sofosbuvir and simeprevir

Sofosbuvir

• NS5B Polymerase Nucleoside Inhibitor
• Potent antiviral activity against HCV GT1–6
• High barrier to resistance
• Oral once a day tablet with no food effect
• No clinically significant drug interactions
• Generally safe and well-tolerated in clinical studies to date (> 3,000 patients)
  – Most common side effects are fatigue and headache
• Treatment in genotypes 1 + 4 is 12 weeks with PEG/RBV
  – Sofosbuvir and RBV for 24 weeks if interferon contraindicated or patient intolerant
• Treatment in genotype 2 is 12 weeks with RBV
• Treatment in genotype 3 is 24 weeks with RBV
• HCV-HIV-1 Co-infection: Safe with multiple antiretroviral agents

**Sofosbuvir**

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

<table>
<thead>
<tr>
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<th>GT1</th>
<th>GT4</th>
<th>GT5,6</th>
<th>Overall</th>
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<tbody>
<tr>
<td>SVR12 (%)</td>
<td>90</td>
<td>96</td>
<td>100</td>
<td>92</td>
</tr>
<tr>
<td>n/N</td>
<td>261/28</td>
<td>27</td>
<td>37/7</td>
<td>295/137</td>
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</table>

No Cirrhosis: 252/273 (92%)
Cirrhosis: 43/54 (80%)

VALENCE: SVR12 With 12 or 24 Wks of SOF + RBV in GT2 and GT3


Simeprevir

- 2nd Generation once a day NS3/4A Protease Inhibitor
- Effective in genotypes 1, 2, 4, 5, 6
- FDA approved for use in genotype 1 only
- No Benefit if Q80K Positive: NS3 Q80K is a naturally occurring polymorphism that occurs in 48% of US genotype 1a
- 61 drug-drug interactions (CYP3A4)
- Adverse reactions: Photosensitivity, rash, pruritus, nausea, myalgia, and dyspnea
- Mild-moderated bilirubin elevations
Simeprevir

- No dose recommendation for hepatic impairment:
  - 2.4-fold higher concentration in moderate hepatic impairment (Child-Pugh Class B)
  - 5.2-fold higher concentration in severe hepatic impairment (Child-Pugh Class C)
- Treatment duration (Uses RGT and a PEG/RBV tail)
  - Treatment naïve and prior relapsers: 12 weeks SMV/PEG/RBV + 12 weeks PEG/RBV
  - Prior non-responders: 48 weeks (12 weeks SMV/PEG/PBV + 36 weeks PEG/RBV)

Simeprevir Naïve Genotype 1 SVR: Pooled Quest 1 and 2

No Benefit if Q80K Positive

GT 1  GT 1a  GT 1b  GT 1a without Q80K  GT 1a with Q80K
80      75    85    84          58

Simeprevir Package Insert November 2013
Simeprevir Treatment Experienced Genotype 1 SVR (Promise Study)

No Benefit if Q80K Positive

GT 1a without Q80K
GT 1a with Q80K
GT 1b

Response-Guided Therapy Paradigm with Simeprevir + Peg INF/RBV in Tx-Naïve + Relapse patients including Cirrhosis

HCV RNA
Detectable or Undetectable (<25IU/ml)
Detectable (>25IU/ml)

Week 0 4 12 24 48

SIM + PEG/RBV
PEG + RBV

Simeprevir Package Insert November 2013
## Treatment Recommendations

### www.hcvguidelines.org

<table>
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<tr>
<th>Genotype</th>
<th>Recommended</th>
<th>Alternative</th>
<th>Not recommended</th>
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<td>1</td>
<td><strong>INF-Eligible</strong></td>
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<tr>
<td></td>
<td>SOF + PEG/RBV x 12 wk</td>
<td>SMV x 12 wk + PEG/RBV x 24 wk in Q80K neg patients</td>
<td>TVR + PEG/RBV</td>
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<td><strong>INF-Ineligible</strong></td>
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</tr>
<tr>
<td></td>
<td>SOF + SMV ± RBV x 12 wk</td>
<td>SOF + RBV x 24 wk</td>
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<td>“This regimen should be considered only those patients who require immediate treatment because it is anticipated that safer and more effective INF-free regimens will be available by 2015.”</td>
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HCV Treatment

The Future

- Shorter treatment duration
- SVR rates of 95+% 
- Fewer adverse events 
- All oral drug combinations for all genotypes

Interferon Free Treatment for HCV

The Holy Grail of Hepatology
(Available starting fall 2014)
WHAT ARE THE PROBLEMS WITH PEGYLATED INTERFERON

**Peginterferon Side Effects**

- **Psychiatric symptoms:**
  - Depression, anxiety, mood changes, suicidal ideation
- **Hematologic side effects:**
  - Anemia, neutropenia, thrombocytopenia
- **Flu-like symptoms:**
  - Headache, fatigue, chills, myalgias, arthralgias
- **GI symptoms:**
  - Nausea, diarrhea, dyspepsia
- Retinopathy
- Thyroid toxicity
Contraindications to Peginterferon

- History of/or ongoing poorly controlled psychiatric disease (depression, bipolar)
- Decompensated cirrhosis
- Autoimmune disease
- Active substance abuse
- Kidney and heart transplants

New HCV Drugs in Development

<table>
<thead>
<tr>
<th>NS3/4A Protease Inhibitors</th>
<th>NS5A Inhibitors</th>
<th>NS5B Polymerase Nucleos(t)ide Inhibitors</th>
<th>Non-Nucleoside NS5B Inhibitors</th>
<th>Host-Targeting Antivirals</th>
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<tr>
<td>Danoprevir</td>
<td>Ledipasvir</td>
<td>ALS-2200</td>
<td>Tegobuvir</td>
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Phase III Studies

Combination Sofosbuvir and Ledipasvir

• Sofosbuvir plus ledipasvir (NS5A inhibitor)
  – Single tablet
• Three phase III studies:
  – Ion I: Genotype 1 naïve with and without cirrhosis
  – Ion II: Genotype 1 treatment experienced
  – Ion III: Genotype 1 naive
ION-1 (Treatment Naïve)

• Sofosbuvir/ledipasvir for 12 weeks: SVR$_{12}$ 99%
  – Cirrhosis present SVR$_{12}$ 94%  Cirrhosis absent SVR$_{12}$ 99%
• Sofosbuvir/ledipasvir/RBV for 12 weeks: SVR$_{12}$ 97%
  – Cirrhosis present SVR$_{12}$ 100%  Cirrhosis absent SVR$_{12}$ 97%
• Sofosbuvir/ledipasvir for 24 weeks: SVR$_{12}$ 98%
  – Cirrhosis present SVR$_{12}$ 94%  Cirrhosis absent SVR$_{12}$ 98%
• Sofosbuvir/ledipasvir/RBV for 24 weeks: SVR$_{12}$ 99%
  – Cirrhosis present SVR$_{12}$ 100%  Cirrhosis absent SVR$_{12}$ 99%
• Conclusion: Adding RBV and/or extending treatment to 24 weeks did not significantly increase SVR$_{12}$
• Adverse events of fatigue, headache and insomnia higher with ribavirin


ION-2 (Treatment-Experienced)

• Sofosbuvir/ledipasvir for 12 weeks: SVR$_{12}$ 94%
• Sofosbuvir/ledipasvir/RBV for 12 weeks: SVR$_{12}$ 96%
• Sofosbuvir/ledipasvir for 24 weeks: SVR$_{12}$ 99%
• Sofosbuvir/ledipasvir/RBV for 24 weeks: SVR$_{12}$ 99%
• Conclusion: Adding RBV and/or extending treatment to 24 weeks did not significantly increase SVR$_{12}$
• No new adverse events with sofosbuvir and ledipasvir
  – Fatigue, nausea, insomnia consistent with ribavirin

Afdhal N et al. EASL 2014 London, April 11, 2014
Afdhal N et al. NEJM Online April 11, 2014
ION-3 (Treatment Naïve without cirrhosis)

- Sofosbuvir/ledipasvir for 8 weeks: SVR$_{12}$ 94%
- Sofosbuvir/ledipasvir/RBV for 8 weeks: SVR$_{12}$ 93%
- Sofosbuvir/ledipasvir for 12 weeks: SVR$_{12}$ 95%

Conclusion: Adding RBV and/or extending treatment to 12 weeks did not increase SVR$_{12}$

- Adverse events of fatigue, nausea, and insomnia were higher in the ribavirin group

Kowedley KV et al. EASL 2014 London, April 10, 2014
Kowedley KV et al. NEJM Online, April 10, 2014

3D plus Ribavirin Combination:

- ABT-450 (protease inhibitor boosted with ritonavir)
- Ombitasvir (NS5A inhibitor)
- Dasabuvir (non-nucleoside polymerase inhibitor)

3 phase III studies:
- SAPPHIRE-I: 12 week treatment in naïve genotype 1, non-cirrhotic patients
- SAPPHIRE-II: 12 week treatment in treatment-experienced genotype 1, non-cirrhotic patients
- TURQUOISE-II: Compensated cirrhotic genotype 1 patients
**SAPPHIRE-I (Treatment Naïve)**

- Overall: SVR$_{12}$ 96.2%
- Genotype 1a: SVR$_{12}$ 95.3%
- Genotype 1b: SVR$_{12}$ 98%
- Similar SVR$_{12}$ rates in all subgroups (sex, race, age, fibrosis stage and viral load)
- Adverse events were generally mild and included fatigue, headache, nausea, and pruritus

Feld JJ et al. EASL 2014 London, April 11, 2014
Feld JJ et al. NEJM Online April 11, 2014

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**SAPPHIRE-II (Treatment Experienced)**

- Overall: SVR$_{12}$ 96.3%
- Genotype 1a: SVR$_{12}$ 96.0%
- Genotype 1b: SVR$_{12}$ 96.7%
- Prior relapsers: SVR$_{12}$ 95.3%
- Prior partial responders: SVR$_{12}$ 100%
- Prior null responders: SVR$_{12}$ 95.2%
- Adverse events were generally mild and included fatigue, headache, nausea, and pruritus

Zeuzem S et al. EASL 2014 London, April 10, 2014
Zeuzem S et al. NEJM Online April 10, 2014
TURQUOISE-II (Compensated Cirrhosis)

- Genotype 1 compensated (Child-Pugh A) cirrhosis, naïve and treatment experienced
- The overall efficacy of 12-week treatment (92%) and 24-week treatment (96%) did not differ significantly
  - 1a patients with a prior null response had a 12 week SVR of 80% and a 24 week SVR of 92.9% suggesting 24 weeks is more effective
- The most common adverse events were fatigue, headache, nausea and pruritus

Poordad F et al. EASL 21014 London, April 12, 2014
Poordad F et al. NEJM Online, April 12, 2014

What Is the Ideal HCV Regimen?

- Highly Effective: High efficacy in all populations including cirrhosis
- All Oral: PegIFN/RBV replaced with alternate backbone with low chance of resistance
- Safe and Tolerable: Few or easily manageable adverse effects
- Simple Regimen: Short duration, simple, straightforward stopping rules
- Pan-Genotypic: Regimen can be used across all genotypes
- Easy Dosing: Once daily, low pill burden
The Price of a Cure: 
DAA is $1,000 a Pill 
SVR is Priceless

Increasing Health Care Costs Associated With Progressive Liver Disease in the Aging HCV-Infected Population

- While the prevalence of HCV infection is declining from its peak, the incidence of advanced liver disease and associated health care costs continue to rise

Healthcare Costs Associated with HCV are Substantial and Increase with Disease Severity


HCV is a Progressive Disease and HCV-Related Healthcare Costs are Directly Related to Disease Severity


HCV Therapy Is Associated with Lower Healthcare Costs and Curing HCV Should Lower Downstream Health Care Costs


NCD=non-cirrhotic disease
CC=compensated cirrhosis
ESLD=end-stage liver disease

![Graph showing cost differences between treated and untreated patients](image)

Predicted cost (2010 $US PPPM)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treated</th>
<th>Untreated</th>
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<tbody>
<tr>
<td>HCV-related</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Medical costs</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Total costs</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>


SVR is Priceless and Cost Effective

- SVR in non-cirrhotic HCV patients prevents the development of cirrhosis and its complications
- SVR in compensated cirrhosis lowers the rate of complications, liver cancer, and transplant
- SVR improves all-cause mortality in all patients
- SVR improves quality of life in all patients
- SVR increases life expectancy

Reau NS, Jensen DM. Hepatology 2014; 59:1246-1249
Treatment with Oral IFN-free Regimens will be the Most Cost-Effective Strategy

• Treatment is short term and curative in almost all patients
• Although DAA is $1,000 a pill ($84,000/12 weeks), the cost is similar to previous 12 week protease inhibitor regimes which have a lower SVR (telaprevir $68,000, PEGINF $12,340)
• There are not as many costs associated with INF-free treatment compared to INF treatment (cost of managing side effects plus $5,000/12 weeks for visits, labs, etc)

Younossi ZM et al. J Hepatology 2014;60:530-537
Pockros P. 29th Annual New Treatments in Chronic Liver Disease, La Jolla, March 29, 2014
Reau, NS, Jenson DM. Hepatology 2014;59:1246-1249

Treatment with Oral IFN-free Regimens will be the Most Cost-Effective Strategy

• The cost of not treating patients is higher than $84,000
  – Patients with compensated cirrhosis may live for over a decade accruing over $270,000 in expense prior to developing end-stage liver disease
  – It markedly reduces the national cost of treating cirrhosis and HCC ($30,000-$70,000 annual cost x 5-10 years/patient)
  – It markedly reduces need for liver transplantation ($350,000/transplant + $145,000 year)

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Pockros P. 29th Annual New Treatments in Chronic Liver Disease, La Jolla, March 29, 2014
Conclusions

• HCV is a major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma
• **Suspect HCV on the basis of risk factors, not symptoms or lab tests**
• **Screen all patients with risk factors, and all baby boomers for HCV**
• We are about to undergo a dramatic paradigm shift in HCV treatment with new DAA combinations that promise higher cure rates, shorter duration and fewer side effects

Questions?