Improving Treatment Success Rates for HCV in a Managed Care Setting

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- Bruce R. Bacon, MD
  - Consultant Fees: Schering Plough/Merck; Gilead Sciences; Three Rivers Pharmaceuticals; Valeant; Vertex; Human Genome Sciences
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Objective

- Assess the clinical challenges of managing patients with hepatitis C virus (HCV) within a managed care setting
Agenda

• Status update: hepatitis C virus (HCV) in 2011
• Complications and mortality of chronic HCV
• Effect of treatment on long-term morbidity and mortality
• Importance of adherence
• Impact of new agents on HCV treatment in managed care
• Summary
HCV Status Update
Majority of Patients Infected With HCV Progress to Chronic Disease

Incubation Period: 14-180 Days Average of 45 Days

Acutely Infected Persons
20% to 30% Develop Symptoms

75% to 80% of Newly Infected Develop Chronic HCV Infections

60% to 70% of Those With Chronic HCV Infections Develop Chronic Liver Disease

10% to 20% With Chronic Liver Disease Develop Cirrhosis Over 20 to 30 Years

Decompensated Cirrhosis
5-year Survival Rate: 50%

Hepatocellular Carcinoma: 1-4% per Year

4% Annual Death Rate Post-Cirrhosis

HCV Is Nearly 4 Times as Prevalent as HIV and HBV

HBV=hepatitis B virus.
HCV=hepatitis C virus.
HIV=human immunodeficiency virus.

Prevalence of Chronic Hepatitis C

- Global prevalence: ~170,000,000 cases
- In the United States:
  - 5 million exposed
  - 3.2 million chronically infected
    - Only 25% of these are aware of their HCV status

Majority of Those With Chronic HCV Are Baby Boomers

Complications and Mortality of Chronic HCV
Cirrhosis Due to HCV Expected to Peak Over the Next Decade

25% of patients with HCV currently have cirrhosis

37% of patients with HCV are projected to develop cirrhosis by 2020, peaking at 1 million

Although a High Number of Men With Chronic HCV are Projected to Develop Cirrhosis….

A Large Number of Women With Chronic HCV Are Projected to Develop Cirrhosis as Well

Complications of Cirrhosis Expected to Increase Over the Next Decade

Men With HCV Have a Greater Burden of Disease Than Women

- Men infected before age 50 show more rapid rates of progression, accounting for 74% of cirrhosis cases in 2009.
- Women infected before age 50 show slower rates of progression and lower risk for developing chronic infection; only 16% had progressed to cirrhosis by 2009.

Cirrhosis Prevalence by Sex and Age at Initial HCV Diagnosis

Failure to Achieve SVR Causes Worsening of Liver Disease

SVR=sustain virologic response.

Mortality Rate Due to HCV in People Over 35 Years

- 123% increase in HCV mortality rates between 1995 - 2004

- Aging of the high prevalence birth cohort (1945-1964) may be reflected in declining mortality seen in the 35-44 age group and an increase in mortality in the 45-64 age group

Effect of Treatment on Long-term Morbidity and Mortality
Why Treat Chronic Hepatitis C?

- **The disease**
  - HCV is common, chronic, and potentially progressive
  - Complications are becoming more common
    - Liver failure
    - Hepatocellular carcinoma (HCC)
- **The treatment**
  - Viral cure, or sustained virologic response (SVR), is achievable
  - SVR associated with histologic improvement and gradual regression of fibrosis\(^1\)
  - SVR leads to lower risk for liver failure and HCC, and improved survival\(^2,3\)

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There Is a Need to Treat More Patients and to Achieve Improved Outcomes

- Disease burden is high and getting worse
- New therapies are becoming available
- Must increase screening efforts to identify more patients for treatment
- Increased sustained virologic response (SVR) means improved outcome
- Adherence leads to an improved SVR

Lower Mortality Results From Improved and Increased HCV Treatment

Successful Treatment Equals SVR

- Sustained virologic response (SVR) – undetectable plasma HCV RNA 24 weeks after completion of treatment – is the goal of therapy\textsuperscript{1,2}

SVR Equals Cure

Nearly 100% of Patients Who Achieve SVR Remain Undetectable During Long-term Follow-up\textsuperscript{1-4}

Histologic Improvement After Successful Anti-HCV Therapy

Pretreatment biopsy: Trichrome stain with Ishak stage 3 fibrosis (portal-to-portal bridging)

Long-term, follow-up biopsy obtained from the same patient 57 months after end of treatment: Trichrome stain with Ishak stage 1 fibrosis

Patient Characteristics Predictive of SVR

- Patients with these characteristics may have a higher likelihood of achieving SVR following treatment with pegylated-interferon and ribavirin:
  - Non-African American race\textsuperscript{1,2}
  - Age <40 years\textsuperscript{1}
  - Lower body weight (\leq 75 kg)\textsuperscript{1,2}
  - Absence of insulin resistance\textsuperscript{1,2}
  - Normal fasting glucose level\textsuperscript{2}
  - Polymorphism in \textit{IL-28B} gene\textsuperscript{3}

• Patients with these disease characteristics may have a higher likelihood of achieving SVR with pegylated-interferon and ribavirin:
  – Non-genotype 1-HCV
  – Low baseline viral load (≤600,000 IU/mL)
  – Absence of bridging fibrosis/cirrhosis
  – Absence of steatosis
  – Elevated baseline ALT (3xULN)

Viral Kinetics Predict SVR

91% of patients who reach undetectable HCV RNA at Week 4 achieved SVR.

RVR=rapid virologic response.

Importance of Adherence to Treatment
# Adherence to Therapy Is Critically Important to Improving Outcomes

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<thead>
<tr>
<th>Treatment</th>
<th>Dosing</th>
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<tbody>
<tr>
<td>Peg-interferon&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Q week</td>
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<tr>
<td>Ribavirin&lt;sup&gt;2&lt;/sup&gt;</td>
<td>BID</td>
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<td>Protease inhibitor</td>
<td>TID</td>
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<tr>
<td>• boceprevir&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Q8 hours</td>
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<tr>
<td>• teleprevir&lt;sup&gt;4&lt;/sup&gt;</td>
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Self-reported Adherence to Treatment With Peg-IFN and RBV

A Multidisciplinary Approach Is Required to Enhance Patient Adherence

- Educate and empower patients about disease state
- Anticipate and manage medication side effects
- Identify financial and psychosocial resources
- Improve dosing strategies

Increased adherence, which results in effective treatment

Impact of New Agents on HCV Treatment in Managed Care
HCV Treatment Continues to Evolve

Infergen 10/97
Rebetol 6/98
PegIntron 1/01
Copegus 12/02
Ribavirin 10/02
Pegasys 1/03
Ribasphere 4/04


Expected telepravir and boceprvir review
Current and Emerging Therapies Will Be Combined to Increase SVR

• Newer agents such as the oral protease inhibitors are emerging

• However, treatment regimens will continue to rely on interferon and ribavirin (RBV) for at least another few years

• Regardless of the regimen, patients must be adherent for efficacy and to prevent/limit resistance

Asselah T, Marcellin P. Liver Int. 201;(31 Suppl 1):68-77.
Ribavirin Is Critical to the Success of HCV Combination Therapy

- **RBV will continue to play an important role in successful antiviral therapy**
  - Antiviral and immunomodulatory activity
  - Reduced likelihood of relapse
- **Can we optimize treatment by fine tuning the use of RBV?**
  - How important is the initial dose of RBV?
  - Do we need to maintain the RBV dose for the duration of treatment?

Cumulative RBV Exposure
>60% of the Initially-assigned Dose

Treatment Weeks 0-12 vs Weeks 0-48

- Standard Dose PegIFNα-2b + RBV
- Low-dose PegIFNα-2b + RBV
- PegIFNα-2a + RBV

Milestones in IFN-based HCV Therapy

RBV in Combination With Interferon-α
Led to Marked Improvements in SVR Rate*

*In patients infected with HCV genotype 1, high viral load.

Reduction of RBV Dose Associated With Stepwise Increase in Relapse Rate

Mean RBV Dose Significantly Correlated With Relapse ($P<.0001$)

**RBV Is Critical for Protease Inhibitor Combination Therapy**

PROVE=Protease Inhibition for Viral Evaluation.
SPRINT=Serine Protease Inhibitor Therapy.


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PROVE-2

- T12PR12 (n=82): 60, 24%
- T12P12 (n=78): 36

PROVE-3

- T24PR48 (n=13): 53, 29%
- T24P24 (n=111): 24

SPRINT-1

- PBR48 (n=103): 67, 31%
- PBLowR48 (n=59): 36
Impact of Newer Agents on HCV Treatment in Managed Care

- Approval of new agents such as the oral protease inhibitors will require HCV treatment guidelines to be updated
  - New guidelines will require managed care reimbursement algorithms to be created to define eligibility criteria
- Stakeholders should work to reduce the lag following approval of these new agents, the revision HCV practice guidelines, and subsequent managed care reimbursement guidance

Summary
Summary

- Prevalence of HCV increasing
- Disease burden can be reduced through better patient identification and treatment designed to increase SVR
- Increased SVR equals improved outcomes
- Adherence is critical for increasing SVR
- Regimens that combine ribavirin with a protease inhibitor improve SVR
- Availability of new agents will require treatment guidelines and managed care reimbursement algorithms to be revised