Have you treated a patient for HCV with an all oral combination?

A. Yes
B. No
Do you think you will treat a patient with HCV with an all oral combination within the next year?

A. Yes
B. No

67% Yes
33% No
Outline

• Epidemiology/National History
• Terminology for Treatment
• Treatment Considerations
• Current Treatment Options
  – Genotype 1 (GT 1)
  – Genotype 2 (GT 2)
  – Genotype 3 (GT 3)
• Cost Wars
Outline

• Epidemiology/National History
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• Cost Wars
Epidemiology of HCV

- ≈ 170 M persons infected worldwide
- 2.7 - 4 M Americans infected
- High prevalence rates in USA
  - 2.5% of males
  - 3.2% of African Americans
  - 2.1% of Hispanic Americans
  - Peak age of persons born between 1945 - 1965

Two-Thirds of Those With Chronic HCV in the U.S. Were Born 1945 - 1965

Estimated Prevalence by Age Group

Natural History of HCV Infection

Recovery & Clearance of HCV (20)

Acute HCV Infection (100)

Chronic Infection (80)

Mild (24)
Moderate (32)
Severe (24)

Chronic Hepatitis
End-Stage Liver Disease
Cirrhosis
Hepatocellular CA

Projected Cases of Hepatocellular Carcinoma & Decompensated Cirrhosis Due to HCV

Gastroenterology 2010;138:513-521
Global Burden Disease Study 2010: Cirrhosis, Liver Cancer, & Death in the US

- Estimated 19,500 liver cancer & 49,500 cirrhosis deaths in US in 2010
- Total liver-related deaths increased from 45,000 to 70,000 over 20 yrs


Causes of CLD Death, US 2010

<table>
<thead>
<tr>
<th>Causes of CLD Death</th>
<th>Deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>16</td>
</tr>
<tr>
<td>Alcohol</td>
<td>41</td>
</tr>
<tr>
<td>HCV</td>
<td>29</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Causes of CLD Death</th>
<th>Deaths (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver cancer–HBV</td>
<td>25,000</td>
</tr>
<tr>
<td>Liver cancer–HCV</td>
<td>20,000</td>
</tr>
<tr>
<td>Liver cancer–alcohol</td>
<td>15,000</td>
</tr>
<tr>
<td>Cirrhosis–HBV</td>
<td>10,000</td>
</tr>
<tr>
<td>Cirrhosis–HCV</td>
<td>5,000</td>
</tr>
<tr>
<td>Cirrhosis–alcohol</td>
<td>0</td>
</tr>
</tbody>
</table>

# Patient Survival Rates with HCV (+) & HCV (−) After Liver Transplantation

<table>
<thead>
<tr>
<th>Year</th>
<th>HCV (+)</th>
<th>HCV (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>4439</td>
<td>6597</td>
</tr>
<tr>
<td>4</td>
<td>3035</td>
<td>4784</td>
</tr>
<tr>
<td>3</td>
<td>1951</td>
<td>3343</td>
</tr>
<tr>
<td>2</td>
<td>1134</td>
<td>2117</td>
</tr>
<tr>
<td>1</td>
<td>519</td>
<td>1003</td>
</tr>
<tr>
<td>0</td>
<td>98</td>
<td>220</td>
</tr>
</tbody>
</table>

Log-rank $X^2 = 19.7$, $P < 0.0001$

Gastroenterology 2002;122:889.
Outline

• Epidemiology/National History
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• Current Treatment Options
  – Genotype 1 (GT 1)
  – Genotype 2 (GT 2)
  – Genotype 3 (GT 3)
• Cost Wars
Liver Fibrosis

Liver biopsy: gold standard

CT, MRI, or US can demonstrate cirrhosis

Fibrosure > 0.48 = F2 or higher

Fibroscan > 7.5 kpascals = F2 or higher
Prevalence of HCV Genotypes (GT) in the USA

- 1a (40%)
- 1b (35%)
- 1a & 1b
- 2a
- 2b
- 3
- 4
**Patterns of Virologic Response**

- **HCV RNA (log$_{10}$ IU/mL)**
  - Undetectable
  - RVR: rapid virological response
  - EVR: early virological response
  - ETR: end of treatment response
  - SVR: sustained virological response

**PegInterferon (IFN) & Ribavirin (RIB)**

- Null Response*
- Partial Response*
- Relapse

*Subset of Nonresponse

- 4 weeks - RVR: rapid virological response
- 12 weeks - eRVR: extended RVR & EVR: early virological response
- 24 - 48 weeks - ETR: end of treatment response
- 24 weeks after treatment - SVR: sustained virological response

Outline

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HCV Life Cycle & DAA Targets


Receptor binding and endocytosis

Fusion and uncoating

Transport and release

Translation and polyprotein processing

NS3/4 protease inhibitors

ER lumen

Membranous web

RNA replication

Virion assembly

NS5B polymerase inhibitors
Nucleoside/nucleotide
Nonnucleoside

Block replication complex formation, assembly

NS5A inhibitors
Mortality & Progression of HCV Chronic Hepatitis Cohort Study (CHeCS)

2004-2011, N = 14,256
Median F/U 4 years

Liver bx N=2110

F2 N= 616 (29%)
F3 N= 336 (16%)
F4 N= 300 (14%)

<table>
<thead>
<tr>
<th>Decompensation 3.6 %</th>
<th>Decompensation 10.1 %</th>
<th>Decompensation 27.7 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCC 1.0 %</td>
<td>HCC 2.7%</td>
<td>HCC 8.3%</td>
</tr>
<tr>
<td>Death 4.9 %</td>
<td>Death 10.4%</td>
<td>Death 23.7%</td>
</tr>
</tbody>
</table>

Receipt of any antiviral therapy was protective, Adjusted Hazard Ratio = 0.7

Moorman Abstract # 174 AASLD 2014
Effects of SVR on the Risk of All Cause Mortality: Meta-analysis of 129 Studies in 23,309 Patients with HCV

5-year All Cause Mortality

<table>
<thead>
<tr>
<th></th>
<th>General</th>
<th>Cirrhotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR</td>
<td>4.5</td>
<td>3.6</td>
</tr>
<tr>
<td>NO SVR</td>
<td>10.5</td>
<td>11.3</td>
</tr>
</tbody>
</table>
Outline

• Epidemiology/National History
• Terminology for Treatment
• Treatment Considerations
• Current Treatment Options
  – Genotype 1 (GT 1)
  – Genotype 2 (GT 2)
  – Genotype 3 (GT 3)
• Cost Wars
NS3/4A Protease Inhibitors
High potency
Limited genotypic coverage (1)
Low barrier to resistance
Direct-Acting Antiviral Agents: Key Characteristics

**NS3/4A Protease Inhibitors**

- High potency
- Limited genotypic coverage (1)
- Low barrier to resistance
- Boceprevir (BOC)
- Telaprevir (TEL)
- Simeprevir (SIM)
- Paritaprevir (PAR)
Direct-Acting Antiviral Agents: Key Characteristics

NS5A Inhibitors
High potency
Multigenotypic coverage
Low barrier to resistance
Direct-Acting Antiviral Agents: Key Characteristics

- **NS5A Inhibitors**
  - High potency
  - Multigenotypic coverage
  - Low barrier to resistance
  - Ledipasvir (LED)
  - Ombitasvir (OMB)
Direct-Acting Antiviral Agents: Key Characteristics

NS5B Nucleos(t)ide Inhibitors
Intermediate potency
Pangenotypic coverage
High barrier to resistance
NS5B Nucleos(t)ide Inhibitors
Intermediate potency
Pangenotypic coverage
High barrier to resistance
Sofosbuvir (SOF)
Direct-Acting Antiviral Agents: Key Characteristics

- **NS5B Nonnucleoside Inhibitors**
- Intermediate potency
- Limited genotypic coverage (1)
- Low barrier to resistance
Direct-Acting Antiviral Agents: Key Characteristics

NS5B Nonnucleoside Inhibitors
Intermediate potency
Limited genotypic coverage (1)
Low barrier to resistance
Dasabuvir (DSV)
Direct-Acting Antiviral Agents: Key Characteristics

NS3/4A Protease Inhibitors
- Simeprevir (SIM)
- Paritaprevir (PAR)

NS5A Inhibitors
- Ledipasvir, (LED)
- Ombitasvir, (OMB)

NS5B Nucleos(t)ide Inhibitors
- Sofosbuvir (SOF)

NS5B Nonnucleoside Inhibitors
- Dasabuvir (DSV)
BOC, boceprevir; DAS, dasabuvir; GT, genotype; IFN, interferon; LED, ledipasvir; OMB, ombitasvir; PAR, paritaprevir; pegIFN, peginterferon; RIB, ribavirin; RIT, ritonavir; SIM, simeprevir; SOF, sofosbuvir; TEL, telaprevir
Sofosbuvir (SOF)

- Oral, once-daily nucleotide NS5B polymerase inhibitor
- Potent antiviral activity; pangenotypic
- High barrier to resistance
- Minimal side effects
- Pharmacology profile
  - Amiodarone can cause serious bradycardia
- Approved for combination treatment of HCV in following settings
  - Genotypes 1, 2, 3, 4 HCV
  - HCC meeting Milan criteria & awaiting transplantation
  - HIV coinfection
- Cost $ 84,000 for 12 weeks
SOF + RIB for 24 Weeks in 60 GT 1 Pts
Intolerable to PegIFN

- No one discontinued treatment due to adverse events.
- Most frequent adverse events were headache, anemia, fatigue & nausea

SOF + PegIFN/RIB for GT1 HCV: FDA Approved Indications

• SOF 400 mg/day with or without food, administered with P/R
• All GT1 patients receive same regimen, regardless of previous treatment history or fibrosis level
  – Same regimen approved for GT4 HCV

12 weeks

Sofosbuvir + P/R $ 94,500

• Additional option for GT1 patients ineligible for IFN therapy
  – Sofosbuvir + ribavirin for 24 weeks $ 183,000

Simeprevir (SIM)

- Oral, once-daily NS3 protease inhibitor for GT1 HCV, which contains a sulfonamide moiety
- Greatly improved adverse effect profile vs previous Protease Inhibitors
  - No anemia
  - SE include rash, jaundice, increase LFTs, sun intolerance
- Moderate drug–drug interactions
  - CYP450 3A pathway
- No data in Child’s B/C patients
- Approved for combination treatment of Genotype 1 HCV
  - Pegylated interferon + Ribavirin (should not used if polymorphism Q80K is present)
  - Sofosbuvir
- Cost $ 66,000 for 12 weeks
COSMOS: SIM + SOF ± RIB in GT 1 HCV Patients

- 2 cohorts with same study design evaluating impact of duration & RIB
- Primary endpoint: SVR12

SIM 150 mg QD; SOF 400 mg QD; weight-based RIB 1000-1200 mg/day.

Simeprevir + Sofosbuvir

- Discontinuation rate < 2%
- Side effects include fatigue (25%), headache (21%), nausea (21%), dizziness (16%), diarrhea (16%), insomnia (14%) pruritus (11%), rash (11%), & photosensitivity (7%)
- FDA approved
  - 12 wks in noncirrhotics (cost $ 150,000)
  - 24 weeks in cirrhotics (cost $ 300,000)
Sofosbuvir/Ledipasvir

- **Ledipasvir**
  - Picomolar potency against genotype 1 HCV\(^1\)
  - Once-daily, oral, 90 mg
  - No significant drug interactions
  - Minimal side effects
- **Ledipasvir/sofosbuvir FDC**
  - Once-daily, oral FDC tablet (90/400 mg)
  - Cost $ 94,500 for 12 weeks

Phase III Studies: SOF/LED ± RIB in GT1 Patients

ION-1\(^1\)
Treatment-naive GT1 HCV; cirrhosis in 15% to 17% per arm (N = 865)
- SOF/LED (n = 214)
- SOF/LED + RIB (n = 217)
- SVR12, %
  - 99
  - 97
  - 98
  - 99

ION-2\(^2\)
Treatment-experienced GT1 HCV; 20% cirrhotics (N = 440)
- SOF/LED (n = 109)
- SOF/LED + RIB (n = 111)
- Wk 12
  - 94
  - 96
  - 99
  - 99

ION-3\(^3\)
Treatment-naive, noncirrhotic pts with GT1 HCV (N = 647)
- SOF/LED (n = 215)
- SOF/LED + RIB (n = 216)
- Wk 8
  - 94
  - 93
  - 95

ION-1: SVR12 According to Cirrhosis Status

SVR12 rates did not differ by GT1a vs GT1b in any treatment arm

ION-2: SOF/LED in Treatment-Experienced Pts With Cirrhosis, GT1 HCV

- Randomized, open-label phase III trial in 88 pts with cirrhosis & previous failure on pegIFN/RIB ± PI

<table>
<thead>
<tr>
<th>Circrhotics per arm</th>
<th>Wk 12</th>
<th>Wk 24</th>
<th>SVR12 in Cirrhotics, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 22</td>
<td>SOF/LED</td>
<td></td>
<td>86</td>
</tr>
<tr>
<td>n = 22</td>
<td>SOF/LED + RIB</td>
<td></td>
<td>82</td>
</tr>
<tr>
<td>n = 22</td>
<td>SOF/LED</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>n = 22</td>
<td>SOF/LED + RIB</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

24 wks needed in treatment-experienced cirrhotics

Safety & DDIs With SOF/LED

- **Safety/tolerability**\(^{[1]}\)
  - Treatment-related AEs: 45% SOF/LED
    - < 1% d/c due to AEs
    - < 1% serious AEs
    - Headache, fatigue: ~ 20%
    - Nausea, diarrhea: ~ 8% to 10%
    - Almost no anemia

- **DDIs**\(^{[2]}\)
  - St John’s wort
  - Rifampin
  - Acid reducing agents: high pH reduces LED absorption
  - Seizure meds: most older meds are contraindicated
  - Anti-retrovirals: most okay; careful with tenofovir & check them all
  - Amiodarone can cause serious bradycardia

1. Alqahtani S, et al. AASLD 2014. Abstract 1944. Note that these data were available in abstract form only at the time of drafting this slideset and are subject to change at the AASLD 2014 presentation.
**SOF/LED: FDA-Approved Indication**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommended Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naive with or without cirrhosis</td>
<td>12 wks* ($94,500)</td>
</tr>
<tr>
<td>Treatment experienced† <em>without</em> cirrhosis</td>
<td>12 wks ($94,500)</td>
</tr>
<tr>
<td>Treatment experienced† <em>with</em> cirrhosis</td>
<td>24 wks ($189,000)</td>
</tr>
</tbody>
</table>

*8-wk duration can be considered in treatment-naive pts without cirrhosis who have pretreatment HCV RNA < 6 million IU/mL.
†Treatment-experienced pts who have failed treatment with pegIFN/RIB ± HCV PI.
SOF/LED ± RIB in Cirrhotics Failed Protease Inhibitors/ PEG INF/RIB

- Randomized, placebo controlled study - Compensated Cirrhotics
- Platelets < 100 K = 18%, serum albumin < 3.5 = 13%
- All, but 1 (sepsis), completed therapy

Bouliere # LB 6, AASLD 2014
SOF/LED + RIB in Cirrhotics Failed Protease Inhibitors/ PEG INF/RIB

- Randomized, placebo controlled study - Compensated Cirrhotics
- Platelets < 100 K = 18%, serum albumin < 3.5 = 13%
- All, but 1 (sepsis), completed therapy

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>12 wks</th>
<th>24 wks SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 77</td>
<td>PLACEBO</td>
<td>SOF + LED + RIB</td>
<td>96%</td>
</tr>
<tr>
<td>N = 77</td>
<td>SOF + LED + PLACEBO</td>
<td></td>
<td>97%</td>
</tr>
</tbody>
</table>

Improved biochemical & synthetic parameters noted
**SOF/LED in G1 CPC B ( Decompensated) Cirrhotics: Open Labeled Trial**

N = 20  →  SOF/LED  →  Wk 12  ↓  SVR12  65% (13/20)

SOF/LED 400 mg/90 mg daily

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>GT1, CTP Class B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median total bilirubin, mg/dL (range)</td>
<td>1.5 (0.7-3.7)</td>
</tr>
<tr>
<td>Median serum albumin, g/dL (range)</td>
<td>3.1 (2.3-3.8)</td>
</tr>
<tr>
<td>Median INR (range)</td>
<td>1.2 (1.0-3.0)</td>
</tr>
<tr>
<td>Ascites, n (%)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Hepatic encephalopathy, n (%)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Median platelet count, 10^3/µL (range)</td>
<td>84 (44-162)</td>
</tr>
</tbody>
</table>

SOF/LED + RIB in G1 or 4 HCV Pts with Decompensated Cirrhosis

• Prospective, Multi-center Randomized Study to 12 or 24 wks of SOF/LED + RIB 600 mg escalation
• MELD > 10 (MELD 16-20 46%)
• Median platelets 71-88 k

<table>
<thead>
<tr>
<th></th>
<th>12 wks</th>
<th>24 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPC B</td>
<td>87/86</td>
<td>89/90</td>
</tr>
<tr>
<td>CPC C</td>
<td>26/24</td>
<td>24/27</td>
</tr>
<tr>
<td>Overall</td>
<td>45/42/26</td>
<td>42/47/24</td>
</tr>
</tbody>
</table>

Flamm, SL, Abstract # 239, AASLD 2014
Paritaprevir/Ritonavir/Ombitasvir + Dasabuvir

- Paritaprevir: potent NS3/4A protease inhibitor
  - Ritonavir boosting to increase peak, trough, & overall exposures of paritaprevir
    - Enables once-daily dosing, but associated with significant drug interactions
- Ombitasvir: potent NS5A inhibitor
  - Co-formulated with paritaprevir/ritonavir
- Dasabuvir: nonnucleoside NS5B polymerase inhibitor
- 5 drugs (3 pills): 3 pills in the AM + RIB, 1 pill in the PM + RIB
- Cost $ 83,400 for 12 weeks
SAPPHIRE I & II: PAT/RIT/OMB + DAS + RIB for 12 Wks in Noncirrhotic Pts

**TURQUOISE-II: PAR/RIT/OMB/DAS + RIB in Cirrhotic GT1 Pts With Prior PegIFN/RIB Failure**

- Randomized, open-label phase III trial in 380 cirrhotic pts
  - n = 220 were previously treated with pegIFN/RIB

<table>
<thead>
<tr>
<th>Group</th>
<th>Tx exp’d per arm</th>
<th>Wk 12</th>
<th>Wk 24</th>
<th>SVR12, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Null responders</td>
<td>n = 75</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td>SVR 80% in GT1a nulls</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>n = 62</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>Partial responders</td>
<td>n = 18</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td></td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>n = 13</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Relapsers</td>
<td>n = 29</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td></td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>n = 23</td>
<td>PAR/RIT/OMB/DAS + RIB</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

- Cirrhotic null responders with GT1a benefit from 24 wks of PAR/RIT/OMB/DAS + RIB

RIB-Free Therapy in GT1b

PEARL-II [1]
- GT1b Tx Experienced
  - PAR/RIT/OMB/DAS (n = 95)
  - PAR/RIT/OMB/DAS + RIB (n = 91)
  - Week 12 SVR12, %
    - 100

PEARL-III [2]
- GT1b Tx Naive
  - PAR/RIT/OMB/DAS (n = 209)
  - PAR/RIT/OMB/DAS + RIB (n = 210)
  - Week 12 SVR12, %
    - 99

PEARL-IV [2]
- GT1a Tx Naive
  - PAR/RIT/OMB/DAS (n = 205)
  - PAR/RIT/OMB/DAS + RIB (n = 100)
  - Week 12 SVR12, %
    - 90

- RIB needed for GT1a, not necessary for GT1b noncirrhotics

Safety With PAR/RIT/OMB/DAS ± RIB

<table>
<thead>
<tr>
<th>Event, %</th>
<th>P/R/O/D+ RIB</th>
<th>P/R/O/D</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>84</td>
<td>75</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Serious AE</td>
<td>2</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Headache</td>
<td>25</td>
<td>26</td>
<td>NS</td>
</tr>
<tr>
<td>Fatigue</td>
<td>29</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>Nausea</td>
<td>14</td>
<td>9</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Pruritus</td>
<td>11</td>
<td>6</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Hemoglobin &lt; 10 g/dL</td>
<td>7</td>
<td>0</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Bilirubin &gt; 3 x ULN</td>
<td>5</td>
<td>0.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

- PAR/RIT/OMB/DAS: significant drug interactions with drugs cleared by CYP3A → check the package insert

### PAR/RIT/OMB/DAS: FDA-Approved Indication

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommended Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1A without cirrhosis *</td>
<td>12 wks* ($90,900)</td>
</tr>
<tr>
<td>Genotype 1A with cirrhosis *</td>
<td>24 wks ($90,900)</td>
</tr>
<tr>
<td>Genotype 1B without cirrhosis</td>
<td>12 wks ($83,400)</td>
</tr>
<tr>
<td>Genotype 1B with cirrhosis *</td>
<td>12 wks ($90,900)</td>
</tr>
</tbody>
</table>

* Also requires ribavirin, if weight < 75 kg 1000 mg per day & if weight > 75 kg 1200 mg per day

Outline

• Epidemiology/National History
• Terminology for Treatment
• Treatment Considerations
• Current Treatment Options
  – Genotype 1 (GT 1)
  – Genotype 2 (GT 2)
  – Genotype 3 (GT 3)
• Cost Wars
VALENCE: SOF + RIB for 12 or 24 Weeks in Naive & Exp’d GT2/3 HCV Pts

- Phase III study in Europe
- Original protocol amended to lengthen treatment for all GT3 pts when emerging data suggested benefit of additional treatment for this group*
- Primary endpoint: SVR12


*Small number of GT3 patients (n = 11) who had already completed 12 wks at time of protocol amendment were included in safety analysis with GT2 but analyzed separately for efficacy. Patients randomized to placebo in original protocol offered alternative treatment protocol.
VALENCE: SVR12 With 12 or 24 Wks of SOF + RIB in GT2 & GT3 Pts

- No increase in AEs seen with longer duration treatment
  - AEs seen consistent with RIB

Sofosbuvir + RIB for GT 2 & 3 HCV: Approved Indications

- All GT2 patients receive same regimen, regardless of previous treatment history or fibrosis level
  - 12 weeks SOF + RIB $ 91,500

- All GT3 patients receive same regimen, regardless of previous treatment history or fibrosis level
  - 24 weeks SOF + RIB $ 183,000
Outline

• Epidemiology/National History
• Terminology for Treatment
• Treatment Considerations
• Current Treatment Options
  – Genotype 1 (GT 1)
  – Genotype 2 (GT 2)
  – Genotype 3 (GT 3)
• Cost Wars
GILEAD’s Sofosbuvir $1,000 a Pill
Costs of Treating Patients with HCV

• If we treat two-thirds of U.S. hepatitis C patients at about $100,000 each would cost the country $200 billion.

• Based on early prescribing trends, analysts predict Sofosbuvir sales in the USA could reach $3 to $10 billion this year. That would shatter the record for first-year sales of any drug & would make Sofosbuvir one of the best-selling drugs in the world (NY Times 3/21/14).
Gilead Chairman & CEO, John Martin

• Base salary $1.58 million/year
• Received $3.4 million bonus in 2012
• Netted nearly $19 million, when he sold 282,242 Gilead shares on 12/12/13 at $73.62, which he bought at $7.63 a share.
• Martin still owns over 4 million shares of Gilead stock.
Hepatitis C "Miracle Drug" Will Cost Americans $84K, Egyptians Only $900

Who says money can’t buy a cure? Taxpayer money will fund much of the drug’s costs in the U.S.

Characterized by inflammation of the liver, Hepatitis C remains one of the most common and dangerous viral epidemics afflicting mankind. Spread via blood-to-blood contact -- typically via unsanitary medical equipment, blood transfusions from a carrier, or sharing of needs during intravenous drug use -- the chronic variant of the disease afflicts an estimated 150-200 million people worldwide, including roughly 3.2 million individuals in the U.S. Symptoms include fatigue, cognitive deficiency, cirrhosis of the liver, and a predisposition to liver cancer.
First Class Ticket to Cairo, Egypt
17 Day Tour of Egypt & Jordan
Tour Pyramids
Tour Nile River & Red Sea
Tour Nile River & Red Sea

$2,199
Four Seasons
Four Seasons

$20,750
Rent a Jeep
Aqua & Luce Restaurant
Aqua & Luce Restaurant

$6,750
90 Days Trip to Egypt

- First class round trip ticket to Cairo $2,260
- Egyptian & Jordan Adventure 17 days $2,199
- Four Seasons, Cairo $20,750
- Jeep rental $7,660
- Lunch & Dinner at Aqua Restaurant $ 6,750
- Sofosbuvir $900 + Ribavirin $900
90 Days Trip to Egypt

- First class round trip ticket to Cairo $2,260
- Egyptian & Jordan Adventure 17 days $2,199
- Four Seasons, Cairo $20,750
- Jeep rental $7,660
- Lunch & Dinner at Aqua Restaurant $ 6,750
- Sofosbuvir & Ribavirin $900

Total: $41,419
Treatment Evolution of HCV

Sustained Viral Response (SVR)

DAA: Direct Acting Antiviral; IFN: Interferon; m: months; RIB: Ribavirin; Peg: Pegylated; PI: Protease inhibitor; w: weeks
Do you think you will treat a patient with HCV with an all oral combination within the next year?

A. Yes
B. No
Hepatitis C Treatment 2015

Conclusions