Best of HCV from AASLD

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Evaluation of Sofosbuvir and Simeprevir-based Regimens in the TRIO Network
Academic and Community Treatment of a Real-world, Heterogeneous Population

Abstract #46

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SOF/PEG/RBV or SOF/SMV +/- RBV for 12 Weeks: SVR 12 For Treatment Naïve GT 1 (ITT)

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SOF/PEG/RBV or SOF/SMV +/- RBV for 12 Weeks:
SVR 12 For Treatment Experienced GT 1 (ITT)

Dieterich D, et al. Abstract #46, AASLD 2014
## Treatment Discontinuation

<table>
<thead>
<tr>
<th>Discontinuation Rates by Reason</th>
<th>GT1 SOF + PEG/RBV</th>
<th>GT1 SMV + SOF +/- RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Events*</td>
<td>2.0% (6)</td>
<td>1.4% (4)</td>
</tr>
<tr>
<td>Non-Adherence</td>
<td>4.1% (12)</td>
<td>1.8% (5)</td>
</tr>
<tr>
<td>Financial</td>
<td>0%</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Total</td>
<td>6.1% (18)</td>
<td>3.6% (10)</td>
</tr>
</tbody>
</table>

*General intolerance, rash

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Summary

- SOF + PEG/RBV lead to 81% SVR12 in treatment naïve GT 1 patients in real world setting
- SOF + PEG/RBV in GT 1 treatment experienced
  - No Phase 3 registration trial was conducted
  - SVR 12 results consistent with what was predicted by FDA
  - Although not shown, cirrhosis was most important predictor of response
  - Safety consistent with clinical trial data

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Abstract #981

A Real Life Experience With the COSMOS Regimen in Genotype 1 Chronic Hepatitis C Treatment: Including Patients With East Asian Ancestry and Decompensated Cirrhosis

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Objectives

• Review the clinical course of HCV GT 1 patients treated with simeprevir (SMV) + sofosbuvir (SOF), once-daily for 12 weeks in a real-life clinical setting

• Examine outcomes in the multiethnic population of Hawaii, including patients with East Asian ancestry and decompensated cirrhosis

# Baseline Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>Total (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>63.3% (n=63)</td>
</tr>
<tr>
<td><strong>Decompensated</strong></td>
<td><strong>18.2% (18/63)</strong></td>
</tr>
<tr>
<td>Asian</td>
<td>38.4% (n=38)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>12.1% (n=12)</td>
</tr>
<tr>
<td>Female</td>
<td>36.4% (n=36)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.5 ± 8.4</td>
</tr>
<tr>
<td>BMI</td>
<td>27.3 ± 5.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>62% (n=61)</td>
</tr>
<tr>
<td>Genotype 1a</td>
<td>62% (n=61)</td>
</tr>
<tr>
<td>IL28B, non-CC</td>
<td>52.4% (22/42)</td>
</tr>
<tr>
<td>Q80K positive</td>
<td>20.6% (7/32)</td>
</tr>
</tbody>
</table>
SMV/SOF for 12 Weeks: SVR12 Rates According to Level of Fibrosis

- Overall: 86.5% (45/52)
- Decompensated Cirrhosis: 100% (9/9)
- Cirrhosis: 85.2% (23/27)
- Non-Cirrhotic: 81.3% (13/16)

SMV/SOF for 12 Weeks: SVR12 Rates According to Prior Treatment Experience, Presence of Cirrhosis and Ethnicity

![Bar chart showing SVR12 rates](image)

- **Overall**
  - Total Patients: 86.5%
  - Cirrhotic Patients: 95.8% 94.7%

- **Prior Treatment**
  - Total Patients: 81.5% 88.9%

- **Asian Ethnicity**
  - Asian: 90%
  - Non-Asian: 84.4%

Abstract #1016

Serious Adverse Events and Hepatic Decompensation in Hepatitis C Virus Infected Patients on Sofosbuvir- and/or Simeprevir-based Therapies

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Methods

- Identify patients who experienced an SAE and/or hepatic decompensation during or up to one month following the end of treatment.

- Two cohorts for analysis
  - Cohort 1: Did not undergo liver transplant
  - Cohort 2: Underwent liver transplant

Non LT Cohort: Cumulative Incidence of Hepatic Decompensation/SAE was 4.1%

- Average of 6.5 weeks passed until 1st episode of decomp/SAE
- Average of 2 episodes per case

LT Cohort: Cumulative Incidence of Hepatic Decompensation/SAE was 28.4%

- Average of 4.3 weeks passed until 1st episode of decomp/SAE
- Average of 2 episodes per case

Conclusions

• Rather than the stage of fibrosis, low hepatic reserve may have increased risk in the non-LT patients

• Based on past and current data, SMV should not be used in Child Pugh Class C patients

• The underlying mechanisms leading to life-threatening adverse events or decompensation from SOF- and/or SMV-containing regimens need to be investigated further
Abstract #81

TURQUOISE-II: Regimens of ABT-450/r/Ombitasvir and Dasabuvir With Ribavirin Achieve High SVR12 Rates in HCV Genotype 1-Infected Patients with Cirrhosis, Regardless of Baseline Characteristics

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Summary

• This multi-targeted, IFN-free regimen of ABT-450/r/ombitasvir and dasabuvir with RBV achieves high SVR12 rates across a broad range of treatment-naïve and treatment-experienced GT1 patients with cirrhosis, irrespective of most host, viral, or disease characteristics
  – 91.6% (239/261) GT1a patients achieved SVR12
  – 99.2% (118/119) GT1b patients achieved SVR12

• In a logistic regression, the only factors associated with a lower likelihood of SVR included GT1a, prior null response to PEG/RBV, and IL28B TT genotype

• Importantly, demographics (eg, age, gender, race, BMI, diabetes), viral factors (baseline HCV RNA), disease related factors (albumin, platelets) were not associated with lower SVR rates
Abstract #82

An Integrated Safety and Efficacy Analysis of >500 Patients with Compensated Cirrhosis Treated with Ledipasvir/ Sofosbuvir with or without Ribavirin

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7. Hôpital Beaujon, University of Paris, Paris, France
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13. Department of Hepatology, Université Paris-René Descartes, Paris, France
14. Beth Israel Deaconess Medical Center, Boston, MA
Methods

• 513 patients with GT 1, compensated cirrhosis
• Pooled data from Phase 2 and 3 LDV/SOF ± RBV studies
  – LONESTAR, ELECTRON, ELECTRON-2, 337-0113, ION-1, ION-2, SIRIUS
## Baseline Demographics

<table>
<thead>
<tr>
<th>Patients, %</th>
<th>Treatment Naïve (n=161)</th>
<th>Treatment Experienced (n=352)</th>
<th>Total (n=513)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>63%</td>
<td>68%</td>
<td>67%</td>
</tr>
<tr>
<td>Black</td>
<td>8%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Asian</td>
<td>17%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>GT 1a</td>
<td>53%</td>
<td>63%</td>
<td>60%</td>
</tr>
<tr>
<td>Prior PI Failure</td>
<td>NA</td>
<td>68%</td>
<td>47%</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>50%</td>
<td>31%</td>
<td>37%</td>
</tr>
<tr>
<td>Ex-US</td>
<td>50%</td>
<td>69%</td>
<td>63%</td>
</tr>
</tbody>
</table>
SVR12: LDV/SOF for 12 vs 24 Weeks in Compensated Cirrhotics

Bourlière M, et al. Abstract #82, AASLD 2014

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>12 Weeks</th>
<th>24 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12 (%)</td>
<td>96</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>Patients</td>
<td>493/513</td>
<td>305/322</td>
<td>188/191</td>
</tr>
</tbody>
</table>
Subgroup Observations

• Among treatment-experienced patients, 12 weeks of LDV/SOF resulted in a 90% SVR rate
  – Adding RBV or extending treatment duration increased this rate to ≥96%

• Platelet count <75 x 10^3/uL was associated with a lower SVR rate among treatment-experienced patients with cirrhosis

Bourlière M, et al. Abstract #82, AASLD 2014
Ledipasvir/Sofosbuvir with Ribavirin for the Treatment of HCV in Patients with Decompensated Cirrhosis: Preliminary Results of a Prospective, Multicenter Study

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4. Gilead Sciences, Raleigh, NC
5. University of Pennsylvania School of Medicine, Philadelphia, PA
6. Beth Israel Deaconess Medical Center, Boston, MA
Study Design

- 108 GT 1 or 4 treatment naïve or treatment experienced patients with decompensated cirrhosis (CPT class B[7-9]) or C[10-12])
- Inclusion/exclusion
  - No history of major organ transplant, including liver
  - No HCC
  - Total bili \(\leq 10\) mg/dL, hemoglobin \(\geq 10\) g/dL
  - \(CL_{cr}\) \(\geq 40\) mL/min, platelets \(>30,000 \times 10^3\)/uL
- Stratified by CPT class B or C
- LDV/SOF + RBV for 12 or 24 weeks
LDV/SOF + RBV in Decompensated Cirrhosis: SVR12

Flamm S, et al. Abstract #239, AASLD 2014
## Overall Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>CPT B</th>
<th>CPT C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, %</td>
<td>12 Weeks (n=30)</td>
<td>24 Weeks (n=29)</td>
</tr>
<tr>
<td>Adverse Events (AE)</td>
<td>97%</td>
<td>93%</td>
</tr>
<tr>
<td>Grade 3-4 AE</td>
<td>7%</td>
<td>28%</td>
</tr>
<tr>
<td>Serious AE</td>
<td>10%</td>
<td>34%</td>
</tr>
<tr>
<td>Serious and Related AEs</td>
<td>7%</td>
<td>0</td>
</tr>
<tr>
<td>Treatment discontinuation due to AE</td>
<td>0</td>
<td>3%</td>
</tr>
<tr>
<td>Death</td>
<td>3%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Related SAEs: Anemia, hepatic encephalopathy, peritoneal hemorrhage

Flamm S, et al. Abstract #239, AASLD 2014
Conclusions

- Extending treatment duration to 24 weeks did not increase SVR rate
- LDV/SOF + RBV for 12-24 weeks was generally safe and well tolerated in CPT class B and C patients
Abstract #196

Efficacy and safety of MK-5172 and MK-8742 ± ribavirin in hepatitis C genotype 1 infected patients with cirrhosis or previous null response: Final results of the C-WORTHY Study (Parts A and B)

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8. INSERM U954, Centre Hospitalier Universitaire de Nancy, Université de Lorraine, Vandoeuvre-les-Nancy, France
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11. Texas Clinical Research Institute, Arlington, TX
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13. Infectious Diseases, Uppsala University, Uppsala, Sweden
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15. Merck & Co., Inc., Whitehouse Station, NJ
Background

• Grazoprevir (MK-5172) is a highly potent HCV-specific NS3/4A protease inhibitor

• Elbasvir (MK-8742) is a highly potent HCV-specific NS5A inhibitor

Treatment-naive, non-cirrhotic
12 weeks ± RBV
(n = 65) Pt. A

HIV/HCV Co-infected
Non-cirrhotic
8-12 weeks ± RBV
(n = 94) Pt. B

Treatment-naive
Cirrhotic
12-18 weeks ± RBV
(n = 123) Pt. B

Null Responders
Cirrhotic / Non-cirrhotic
12-18 weeks ± RBV
(n = 130) Pt. B

Lawitz E, et al. Abstract #196, AASLD 2014
SVR12 Rates in Cirrhotic Treatment-naïve and Null Responder GT 1 Patients

<table>
<thead>
<tr>
<th></th>
<th>Treatment-naïve patients with cirrhosis</th>
<th>PR-Nulls with or without cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 Weeks</td>
<td>18 Weeks</td>
</tr>
<tr>
<td>+ RBV</td>
<td>90 (95% CI)</td>
<td>97 (95% CI)</td>
</tr>
<tr>
<td>No RBV</td>
<td>97 (95% CI)</td>
<td>97 (95% CI)</td>
</tr>
<tr>
<td></td>
<td>12 Weeks</td>
<td>18 Weeks</td>
</tr>
<tr>
<td>+ RBV</td>
<td>94 (95% CI)</td>
<td>94 (95% CI)</td>
</tr>
<tr>
<td>No RBV</td>
<td></td>
<td>91 (95% CI)</td>
</tr>
<tr>
<td></td>
<td>12 Weeks</td>
<td>18 Weeks</td>
</tr>
<tr>
<td>+ RBV</td>
<td>100 (95% CI)</td>
<td>97 (95% CI)</td>
</tr>
<tr>
<td>No RBV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lawitz E, et al. Abstract #196, AASLD 2014
Summary

• SVR12 was 92% (23/25) in null responders with cirrhosis treated for 12 weeks with grazoprevir + elbasvir ± RBV

• High efficacy was achieved regardless of the presence or absence of RBV or extended treatment duration from 12 to 18 weeks

• Grazoprevir + elbasvir were generally safe and well tolerated
The Use of All Oral Regimens for Treatment of Chronic Hepatitis C (CHC) Coupled with Birth Cohort Screening Is Highly Cost Effective: The Health and Economic Impact on the U.S. Population

Zobair Younossi\textsuperscript{1,3}; Mendel Singer\textsuperscript{2}; Linda Henry\textsuperscript{3}; Sharon L. Hunt\textsuperscript{1,3}; Thomas Jeffers\textsuperscript{1,3}; Spencer Frost\textsuperscript{1,3}; Brian P. Lam\textsuperscript{1}

1. Center for Liver Disease, Department of Medicine, Inova Fairfax Hospital, Falls Church, VA
2. Health Services Research and Policy, Case Western University, Cleveland, OH
3. Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA
Background & Aims

• As new treatments for HCV are being developed, it is important that these regimens are assessed beyond the cost of a pill and assessed for their “cost per cure” and incremental cost effectiveness ratio (ICER)

• The economic impact of an effective screening strategy followed by highly effective treatment of HCV(+) patients with all oral anti-HCV regimens have not been fully evaluated
Methods

• The cost and health benefits of a hepatitis C screening/treatment program were examined by computer simulation.

• The birth cohort (1945-1965) was modeled over time using a Markov decision analytic model.

• Health outcomes and costs were compared between Birth Cohort Screening and Risk-Based Screening.
Results

• Birth cohort screening followed by treating all HCV positive patients with all oral anti-HCV regimens save more than 4 million life years at an incremental cost of ~37,000 per QALY

• This strategy is the most cost-effective strategy from the societal perspective (ICER<$50,000 per QALY)

• Even when considering a very pessimistic scenario, birth cohort screening-treat all strategy remains the most cost-effective strategy