EXPERT PERSPECTIVES
BEST OF HCV: 2015 YEAR-END UPDATE
PRESENTED IN SPANISH

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This enduring activity is supported by educational grants from AbbVie, Bristol-Myers Squibb, and Gilead Sciences, Inc.
Topics of Discussion

• Chronic Hepatitis C, Cirrhosis and Hepatocellular Carcinoma

• Real World Experience: DAAs Approved in Different Countries

• Late-Stage Grazoprevir/Elbasvir Pangentotypic Fixed Dose Combination Regimen: Dual Therapy

• Late Stage Sofosbuvir Pangentotypic Fixed Dose Combination Regimen: Dual Therapy
Chronic Hepatitis C, Cirrhosis and Hepatocellular Carcinoma
Abstract #88


Prowpanga Udompap¹, Ajitha Mannalithara¹, Nae-Yun Heo¹, Donghee Kim¹, W. Ray Kim¹

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Methods

• Using the National Health and Nutrition Examination Survey (NHANES) data, the investigators identified participants with detectable HCV RNA and assessed liver fibrosis using validated surrogate indicators, including APRI and FIB-4 scores.

• The prevalence of cirrhosis was determined for survey participants for Era 1 (1988-94), Era 2 (1999-2006) and Era 3 (2007-12).
Results

- Out of 52,644 participants with age ≥20, 736 (1.4%) had HCV.
- Based on APRI score, 6.6% (95%CI:2.2-11.0) of US adults with HCV infection in Era 1, 7.6% (95%CI:3.4-11.8) in Era 2 and 17.0% (95%CI:8.0-26.0) in Era 3 were estimated to have cirrhosis (Ishak stage 5-6).
- The prevalence of advanced fibrosis (Ishak stage 4-6) based on FIB-4 was 8.6%, 10.1%, and 16.0% for Eras 1, 2, and 3, respectively.
- The higher prevalence of cirrhosis (determined by APRI) in the recent era was associated with increasing age (OR=1.04, 95%CI:1.02-1.07), diabetes (OR=2.33, 95%CI:1.01-5.40) and obesity (OR=2.96, 95%CI:1.15-7.57).
- When FIB-4 score was used, advanced fibrosis was associated with increasing age (OR=1.08, 95%CI:1.05-1.11) and diabetes (OR=3.37, 95%CI:1.24-9.5).

Conclusion

• Nearly one in five US adults with HCV infection has cirrhosis.

• The prevalence of cirrhosis is rising over time, which is in part attributable to the increasing age of the birth cohort with HCV infection.

• In addition, comorbidities such as diabetes and obesity accelerate liver fibrosis.

• These data further underscore the current recommendations for HCV screening in asymptomatic individuals and highlights the need for systematic assessment for liver fibrosis and comprehensive medical management in those with HCV infection.

Incidence and Predictors of Hepatocellular Carcinoma Following Sustained Virological Response: A National Cohort Study

Hashem B. El-Serag, Peter Richardson, Fasiha Kanwal

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Methods

- US national Veteran's Affairs HCV Clinical Case Registry
  - Patients with positive HCV RNA
  - 10/1999 and 8/2009
  - Follow up through 1/2010
- HCV treatment (PEG +/- RBV)
- SVR: RNA test negative at least 12 weeks after the end of treatment
- Outcome: new HCC after end of treatment
- Potential HCC risk predictors
  - Baseline demographic, virological and clinical features
  - Diabetes defined as time varying variable
  - Cox proportional hazards models (with death as a competing risk)
Results: HCC Incidence Rates in SVR vs no SVR

• The incidence rate of HCC in patients with SVR 3.27/1000 PY (0.327% per year)

• The incidence rate of HCC in patients with no SVR was 13.2 per 1000 PY (1.32% per year)

• HR of 0.358 for SVR vs. no SVR
## Predictors of HCC After SVR: Cox PH model adjusting for the competing risk of death

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cirrhosis at SVR</strong></td>
<td>4.45 (2.53 - 7.82)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Age at SVR (ref &lt;55)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55 - 64</td>
<td>2.40 (1.53 - 3.77)</td>
<td>0.0002</td>
</tr>
<tr>
<td>65+</td>
<td>4.69 (2.04 - 10.78)</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>DM (time varying)</strong></td>
<td>2.07 (1.35 - 3.20)</td>
<td>0.0010</td>
</tr>
<tr>
<td><strong>HCV Genotype (ref GT 1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.56 (0.32 - 1.01)</td>
<td>0.0522</td>
</tr>
<tr>
<td>3</td>
<td>1.91 (1.14 - 3.18)</td>
<td>0.0131</td>
</tr>
</tbody>
</table>
Conclusions

• The risk of HCC after HCV cure, while considerably reduced, remains relatively high at 0.33% per year

• Older age and/or presence of cirrhosis at the time of SVR are associated with a high HCC risk
  – Warrant continued HCC surveillance
  – Treat and cure early and young

• Diabetes is also a risk factor for post SVR HCC
Real World Experience:
DAAs Approved in Different Countries
Abstract #37

Safety and Efficacy of Daclatasvir plus Sofosbuvir with or Without Ribavirin for the Treatment of Chronic HCV Genotype 3 Infection: Interim Results of a Multicenter European Compassionate Use Program

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13. Bristol-Myers Squibb, Hopewell, NJ
14. Bristol-Myers Squibb, Princeton, NJ
Background

• Treatment of HCV genotype (GT) 3-infected patients is a challenge, with urgent need of effective antiviral therapies¹

• The pan-genotypic, 12-week, all-oral, RBV-free regimen of DCV and SOF achieved 96% SVR12 rates in GT 3-infected noncirrhotic patients (ALLY-3)²

• Optimized treatment for GT 3-infected patients with advanced liver disease remains a medical need

• Here we report interim findings on the combination of DCV + SOF ± RBV in HCV GT 3-infected patients with advanced liver disease enrolled in the European DCV compassionate use program (CUP; A1444-237)³
**Primary objective:** To provide access to DCV to patients with life-threatening chronic HCV infection who have no other treatment options

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Week 24*</th>
<th>Week 36</th>
<th>Week 48</th>
<th>Week 72</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV (60mg)* ± SOF (400mg) ± RBV#</td>
<td>Follow-Up</td>
<td>Additional Optional Follow-Up</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Inclusion criteria**
- Age $\geq$ 18 years with no treatment options
- High risk of hepatic decompensation or death within 12 months if left untreated

**Exclusion criteria**
- Creatinine clearance $\leq$ 30 mL/min
- Pregnancy or not using contraception

* Dose adjusted for concomitant ARVs
# Addition of RBV and shorter duration of treatment at the discretion of the physician
‡ HCV RNA < LLOQ, TD or TND at post treatment Week 12 (next value carried backward approach)
SVR12: DCV + SOF +/- RBV in GT3 Patients With Advanced Liver Disease

Not Achieving SVR12

<table>
<thead>
<tr>
<th>Category 1</th>
<th>DCV + SOF</th>
<th>DCV + SOF + RBV</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>% + 95% Cl</td>
<td>86</td>
<td>88</td>
<td>87</td>
</tr>
<tr>
<td>HCV RNA &lt; LLOQ, TD or TND</td>
<td>42/49</td>
<td>29/33</td>
<td>71/82</td>
</tr>
</tbody>
</table>

Breakthrough: confirmed on-treatment HCV/RNA $\geq 1 \log_{10}$ IU/mL over nadir, or $\geq$ LLOQ, if previously $<$ LLOQ, TD or TND; Relapse: confirmed HCV RNA $>$ LLOQ during any posttreatment visit following HCV RNA $<$ LLOQ, TD or TND, at end-of-treatment; Death*: includes 1 patient who died during follow-up period; HCV RNA $<$ LLOQ at post-treatment Week 10.
## Safety Summary

<table>
<thead>
<tr>
<th>Patient, n (%)</th>
<th>DCV + SOF N = 62</th>
<th>DCV + SOF + RBV N = 40</th>
<th>All Patients N = 102</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total AEs</td>
<td>40 (65)</td>
<td>28 (70)</td>
<td>68 (67)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related serious AEs</td>
<td>14 (23)</td>
<td>7 (18)</td>
<td>21 (21)</td>
</tr>
<tr>
<td>AEs leading to discontinuation or death</td>
<td>3 (5)</td>
<td>3 (8)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (3)</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Most frequent AEs (&gt;5% of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>8 (13)</td>
<td>4 (10)</td>
<td>12 (12)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (6)</td>
<td>6 (15)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Anemia</td>
<td>2 (3)</td>
<td>11 (28)</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Treatment-emergent grade 3 or 4 laboratory abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin &lt; 90 g/L</td>
<td>3 (5)</td>
<td>4 (11)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>ALT &gt; 5 x ULN</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AST &gt; 5 x ULN</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total bilirubin &gt; 2.5 x ULN</td>
<td>1 (2)</td>
<td>4 (15)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Creatinine &gt; 1.8 x ULN</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Summary and Conclusion

• In a real-life clinical setting, DCV + SOF ± RBV achieved high SVR rates (87%) in HCV GT 3—infected patients at high risk of hepatic decompensation or death
  – 87% SVR12 in cirrhotic patients (including decompensated cirrhosis)
  – Comparable SVR12 rates with or without RBV in the regimen
• Improvements in liver function were observed
• DCV + SOF ± RBV was generally safe and well tolerated
  – Few discontinuations due to AEs, treatment-related serious AEs, or grade 3/4 laboratory abnormalities
• These findings suggest that DCV + SOF ± RBV is an effective and well tolerated oral treatment for patients with GT 3 infection, including those with most advanced disease
Abstract #204

Impact of Sofosbuvir-Based Regimens on Renal Function in Liver Transplant Recipients: Results of a Multicenter Study

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10. Memorial University, St. John’s, NF, Canada
Background

• The first nucleotide NS5B polymerase inhibitor, sofosbuvir (SOF), is not recommended for patients with severe renal impairment due to pharmacokinetic studies demonstrating higher serum drug and metabolite levels in such patients.

• However, renal function in cirrhotic and non-cirrhotic patients treated with SOF-based regimens is often compromised yet poorly assessed.

• This analysis aims to assess the impact of SOF-based regimens on renal function in liver transplant (LT) recipients with recurrent HCV, and to assess the role of renal function on the efficacy and safety of these regimens.
Methods

• 165 LT recipients across Canada with HCV recurrence were treated with SOF-based regimens from January 2014 to May 2015. Mean patient age was 58±6.85 years; the majority were male, GT1, Caucasian and treatment-experienced.

• One third had aggressive HCV in the graft; 50% had F3/4 fibrosis. The majority were on tacrolimus based immunosuppression. Median time from LT to treatment was 27 (1-309) months.

• Baseline eGFR was calculated by Modification of Diet in Renal Disease formula (MDRD) and patients were stratified into 3 groups: eGFR<30, 30-60 and >60 ml/min.

• The primary outcome was post treatment changes in renal function from baseline.

• Secondary outcomes included SVR12, anemia related AEs, need for blood transfusions or growth factors, serious AEs, treatment discontinuation due to AE, or death.
Results

• An improvement in post treatment renal function was seen in the majority (58%) of patients, mostly in the SVR12 group (81% vs. 19%).

• A decline in renal function seen in 22%; more marked in poorest renal function (eGFR <30), advanced cirrhosis (p=0.01) and prior treatment experience (p=0.03).

• High SVR12 rates (75-85%) were seen across all renal function strata.

• Cirrhotic patients with eGFR <30 had SVR12 rates comparable to the overall patient group. Lower SVR12 rates were seen in cirrhotic vs. non-cirrhotic patients irrespective of baseline eGFR (79% vs. 95% p=0.006).

• Rates of anemia related AEs and transfusion requirement increased across decreasing eGFR strata, notably more in ribavirin based regimens. Immunosuppression had no impact on renal function.
Conclusions

• SOF-based regimens improved overall renal function in liver transplant recipients with SVR, suggesting an association of subclinical HCV-related renal disease.

• SVR12 rates (75-85%) were comparable regardless of baseline renal function but lower in cirrhosis.

• Rates of transfusion and worsening renal function increased with decreasing eGFR.
Failure with All-Oral DAA Regimens: Real-World Experience from the TRIO Network

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4. Northwestern University, Chicago, IL
5. Swedish Medical Center, Seattle, WA
6. Trio Health Analytics, La Jolla, CA
7. Inova/Fairfax Hospital, Fairfax, VA
8. The Queen’s Medical Center, Honolulu, HI
Background

- Data were collected from US providers and specialty pharmacies through a cloud-based disease management program.
- 43% of patients treated at academic institutions and 57% of patients treated in community practices
- All patients treated for 12 weeks
- Regimens studied
  - SOF/LDV
  - SOF/LDV + RBV
  - SMV + SOF +/- RBV
  - VKP +/- RBV (Viekira Pak; AbbVie regimen)
SVR12 Rates by Regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Relapse</th>
<th>Death</th>
<th>LTFU</th>
<th>DC</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDV-SOF</td>
<td>44</td>
<td>3</td>
<td>33</td>
<td>9</td>
<td>1432/1521</td>
</tr>
<tr>
<td>LDV-SOF + RBV</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>74/76</td>
</tr>
<tr>
<td>SMV + SOF +/- RBV</td>
<td>5</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>32/41</td>
</tr>
<tr>
<td>VKP +/- RBV</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>43/47</td>
</tr>
</tbody>
</table>

Afdhal NH, et al. Abstract #LB-17, AASLD 2015
SVR12 Rates by Fibrosis Level

Non-Cirrhotic

- LDV-SOF: 96% (991/1035)
- LDV-SOF+RBV: 100% (45/45)
- SMV+SOF+/-RBV: 76% (16/21)
- VKP+/-RBV: 95% (35/37)

Cirrhotic

- LDV-SOF: 90% (405/448)
- LDV-SOF+RBV: 94% (29/31)
- SMV+SOF+/-RBV: 78% (14/18)
- VKP+/-RBV: 71% (5/7)
Summary/Conclusions

- Overall SVR in US real world GT1 patients is 94% across all DAA therapies.

- Platelets <100k/ml, cirrhosis, prescribing outside of FDA guidelines, and males all had a positive association with treatment failures.

- Practice type, ethnicity, genotype subtype, baseline viral load, post transplant, age, treatment status, and HIV had no clear association with treatment failures.

- Overall discontinuation rate was <1% (12/1685).

Afdhal NH, et al. Abstract #LB-17, AASLD 2015
Late-Stage Grazoprevir/Elbasvir Pangenotypic Fixed Dose Combination Regimen: Dual Therapy
Abstract #42

An Integrated Analysis of 402 Compensated Cirrhotic Patients with HCV Genotype (GT) 1, 4 or 6 Infection Treated with Grazoprevir/Elbasvir

Ira M. Jacobson¹, Eric Lawitz², Paul Y. Kwo³, Christophe Hezode⁴, Cheng-Yuan Peng⁵, Anita Y. Howe⁶, Peggy Hwang⁶, Janice Wahl⁶, Michael Robertson⁶, Eliav Barr⁶, Barbara A. Haber⁶

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⁴. Henri Mondor Hospital, Creteil, France
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⁶. Merck & Co., Inc., Kenilworth, NJ
Background

- Fixed-dose combination tablet administered once daily, without regard to food intake
  - Retains *in vitro* activity against many clinically relevant RAVs\(^1\)\(^-\)\(^3\)
  - Efficacious in treatment-naive & treatment-experienced cirrhotic and non-cirrhotic patients with HCV, and in HIV/HCV co-infected patients \(^4\)\(^-\)\(^7\)

- Grazoprevir steady state AUC\(_{0-24}\) pharmacokinetics
  - \(~65\%\) increase in Childs-Pugh A compensated cirrhotic patients compared to non-cirrhotic patients

**Aim:** to describe the efficacy and safety profile of elbasvir/grazoprevir + RBV among patients with HCV genotype 1, 4, or 6 infection and compensated Childs-Pugh A cirrhosis enrolled in Phase 2/3 clinical trials

### Integrated Analysis of Patients with Cirrhosis in Six Studies (N=402)

<table>
<thead>
<tr>
<th>Treatment naïve patients</th>
<th>Treatment experienced patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12 week treatment duration</strong></td>
<td><strong>12/16/18 week treatment durations</strong></td>
</tr>
<tr>
<td>N=169</td>
<td>N=233</td>
</tr>
</tbody>
</table>

#### Treatment-naïve Patients
- PN 035* | C-WORTHY
  - Treatment-naïve (n=60)
- PN 052 | C-SURFER
  - CKD 4/5 (n=4)
- PN 060 | C-EDGE TN
  - Treatment-naïve (n=70)
- PN 061 | C-EDGE HIV
  - HCV/HIV coinfected (n=35)

#### Treatment-experienced Patients
- PN 048* | C-SALVAGE
  - Prior DAA failures (n=34)
- PN 068 | C-EDGE TE
  - Treatment-experienced (n=147)

1.*GZR + EBR separate entities used in PN035 and PN048: all other studies used FDC
Conclusions

• In compensated cirrhotic patients who are either treatment-naïve or treatment-experienced, a regimen of EBR/GZR was highly efficacious

  – Treatment naïve
    • 12 weeks, no RBV: SVR12 in GT1a, GT1b and GT4=97-100%

  – Treatment experienced
    • 12 weeks, no RBV: SVR12 in prior PR relapsers=100%
    • 16/18 weeks + RBV: SVR12 in prior PR nonresponders GT1, GT4, GT6=100%

• Efficacy was high among TN and TE compensated cirrhotic subjects regardless of platelet count or fibroscan score

• In cirrhotic patients, EBR/GZR was generally safe and well tolerated
Late Stage Sofosbuvir Pangenotypic Fixed Dose Combination Regimen: Dual Therapy
Abstract #LB-2

A Phase 3 Double-Blind Placebo-Controlled Evaluation of Sofosbuvir/Velpatasvir Fixed Dose Combination for 12 Weeks in Naïve and Experienced Genotype 1, 2, 4, 5, 6 HCV Infected Patients with and Without Cirrhosis: Results of the ASTRAL-1 Study

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9. University of Hong Kong, Hong Kong, Hong Kong
10. The Chinese University of Hong Kong, Hong Kong, Hong Kong
11. Santa Maria Annunziata Hospital, Firenze, Italy
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14. University of Alberta, Edmonton, AB, Canada
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17. Gilead Sciences, Inc., Foster City, CA
18. Mount Sinai Beth Israel Medical Center, New York, NY
19. Johann Wolfgang Goethe University Medical Center, Frankfurt, Germany
**Background**

- **Sofosbuvir (SOF)\(^1,2\)**
  - Potent antiviral activity against HCV GT 1–6
  - Once-daily, oral, 400-mg tablet

- **Velpatasvir (VEL; GS-5816)\(^3-5\)**
  - Picomolar potency against GT 1–6
  - 2\(^{nd}\)-generation inhibitor with improved resistance profile

- **SOF/VEL FDC**
  - Once daily, oral, FDC (400/100 mg)

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The ASTRAL Program

SOF/VEL (400 mg/100 mg) 12 Weeks

ASTRAL-1
GT 1, 2, 4–6

ASTRAL-2
GT 2

ASTRAL-3
GT 3

ASTRAL-4
GT 1–6
CPT-B Cirrhosis
Results: SVR12 by Genotype
ASTRAL-1, SOF/VEL

Error bars represent 95% confidence intervals.
Results: SVR12 by Cirrhosis or Prior Treatment
ASTRAL-1, SOF/VEL

Error bars represent 95% confidence intervals.
Abstract #LB-13

Sofosbuvir/Velpatasvir Fixed Dose Combination For The Treatment Of HCV In Patients With Decompensated Liver Disease: The Phase 3 ASTRAL-4 Study


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8. Texas Liver Institute, University of Texas Health Science Center, San Antonio, TX
9. Mount Sinai Hospital, New York, NY
10. New York University School of Medicine, New York, NY
11. University of Michigan, Ann Arbor, MI
12. University of Miami, Miami, FL
13. University of North Carolina at Chapel Hill / UNC School of Medicine, Chapel Hill, NC
14. Gilead Sciences Inc., Foster City, CA
15. Columbia University Medical Center/ New York Presbyterian, New York, NY
16. Beth Israel Deaconess Medical Center, Boston, MA
Background

• HCV-infected patients with decompensated liver disease have significant morbidity and mortality with limited HCV treatment options.

• Velpatasvir (VEL, formerly GS-5816), is a pangenotypic HCV NS5A inhibitor that has demonstrated high SVR rates in patients with genotypes 1-6 HCV infection when used in combination with sofosbuvir (SOF).
SVR12 by Genotype and Regimen

<table>
<thead>
<tr>
<th>SVR 12</th>
<th>SOF/VEL 12 wk</th>
<th>SOF/VEL+RBV 12 wk</th>
<th>SOF/VEL 24 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>75/90</td>
<td>82/87</td>
<td>83/94</td>
</tr>
<tr>
<td></td>
<td>86/86</td>
<td>92/96</td>
<td>86/94</td>
</tr>
<tr>
<td>GT1</td>
<td>60/68</td>
<td>65/68</td>
<td>65/71</td>
</tr>
<tr>
<td></td>
<td>88/96</td>
<td>92/96</td>
<td>88/94</td>
</tr>
<tr>
<td>GT3</td>
<td>7/14</td>
<td>11/13</td>
<td>50/50</td>
</tr>
<tr>
<td></td>
<td>6/12</td>
<td>50/50</td>
<td>50/50</td>
</tr>
<tr>
<td>GT 2, 4, and 6</td>
<td>100/100</td>
<td>100/100</td>
<td>86/94</td>
</tr>
</tbody>
</table>

GT2: 2/4, 4/4, 3/4
GT4: 2/2, 4/4
GT6: 1/1

CPT Score Change From Baseline
ASTRAL-4: Subjects with SVR12, Overall

Patients (%)

<table>
<thead>
<tr>
<th>Change in CPT score</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>1</td>
</tr>
<tr>
<td>-4</td>
<td>1</td>
</tr>
<tr>
<td>-3</td>
<td>5</td>
</tr>
<tr>
<td>-2</td>
<td>29</td>
</tr>
<tr>
<td>-1</td>
<td>72</td>
</tr>
<tr>
<td>0</td>
<td>99</td>
</tr>
<tr>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td>&lt;1</td>
<td>1</td>
</tr>
</tbody>
</table>

Total n=234; 5 patients had no follow-up Week 12 assessment.
MELD Change (Baseline to FU12)
ASTRAL-4: Subjects with SVR12, Overall

Baseline MELD <15
n=208*

52% Improved

27% Worsened

Baseline MELD ≥15
n=26†

84% Improved

8% Worsened

No follow-up Week 12 assessment for *5 patients, †0 patients.
Summary/Conclusions

• Treatment with SOF/VEL for 12 or 24 weeks or SOF/VEL + RBV for 12 weeks resulted in high SVR12 rates in HCV patients with decompensated liver disease
  – SOF/VEL + RBV resulted in SVR12 rates of 96% in HCV GT 1, 85% in GT 3, and 100% in GT 2 and 4

• Among patients who achieved SVR12, virologic response was associated with improved MELD and CPT scores largely due to decreased bilirubin and improvement in synthetic function (albumin)

• SOF/VEL for 12 or 24 weeks or SOF/VEL + RBV for 12 weeks was safe and well tolerated, with AEs consistent with clinical sequelae of advanced liver disease and RBV toxicity
This enduring activity is supported by educational grants from AbbVie, Bristol-Myers Squibb, and Gilead Sciences, Inc.