Addressing Unmet Medical Needs in HCV Genotype 3

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Department of Medicine
University of Alberta
Objectives

• Identify treatment options available to various patient populations with HCV genotype (GT) 3

• Review efficacy, safety, and tolerability data of different therapeutic options

• Recognize the expanding treatment armamentarium of HCV
## Conflicts of Interest

<table>
<thead>
<tr>
<th>Dr. Karen Doucette</th>
<th>Dr. Duncan Webster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advisory Board / Consultant</td>
<td>AbbVie</td>
</tr>
<tr>
<td>Speaker’s Bureau</td>
<td></td>
</tr>
<tr>
<td>Grants / Honorarium</td>
<td>Gilead, Hoffmann-LaRoche</td>
</tr>
<tr>
<td>Clinical Trial Involvement (Within Past Two Years)</td>
<td>AbbVie, BMS, Gilead, Janssen, Merck</td>
</tr>
</tbody>
</table>
HCV Therapy
Past, Present, and Future

1991: Standard interferon
1998: Interferon + ribavirin
2001: Interferon + ribavirin

2011: Simeprevir or sofosbuvir + P/R
2013: Boceprevir or telaprevir + P/R

2014: IFN-free DAA combinations (GT 1)

2013: Sofosbuvir + ribavirin
2015-: Next generation DAA combinations (GT 3)
HCV GT 3
Pathogenesis

- GT 3 HCV is most pathogenic
  - Increased risk of cirrhosis and hepatocellular carcinoma
- HCV infection associated with steatosis and requires lipids for replication and assembly; the host serum lipid profile is modified by HCV
- Direct involvement of HCV
  - Steatosis is more frequent and severe in patients with GT 3 HCV
  - The severity of steatosis correlates with HCV RNA levels in patients with GT 3 infection
  - Steatosis decreases with successful antiviral therapy
  - In HCV-infected patients, steatosis due to metabolic syndrome is associated with increased liver disease progression and reduced response to therapy
- With this, and recent changes in HCV treatment, GT 3 is now the most difficult HCV infection to treat

Case 1: Naïve

- 41M with GT 3 HCV
- Treatment naïve
- Comorbidities: obesity (BMI 35), schizophrenia
- Meds: risperidone, clonazepam, methadone
- FibroScan® 8.4 kPa (F2 fibrosis)
FISSION
Poorer Response to SOF/RBV in GT 3 vs. GT 2 Naïves, Especially Cirrhotics

All Patients

<table>
<thead>
<tr>
<th></th>
<th>GT 2</th>
<th>GT 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR&lt;sub&gt;12&lt;/sub&gt; (%)</td>
<td>68/70</td>
<td>102/183</td>
</tr>
<tr>
<td>n/N</td>
<td>52/67</td>
<td>110/176</td>
</tr>
</tbody>
</table>

Patients With Cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>GT 2</th>
<th>GT 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR&lt;sub&gt;12&lt;/sub&gt; (%)</td>
<td>10/11</td>
<td>13/38</td>
</tr>
<tr>
<td>n/N</td>
<td>8/13</td>
<td>11/37</td>
</tr>
</tbody>
</table>

Impact of Cirrhosis and Duration on SVR Rates

FUSION

GT 3

Sofosbuvir + RBV 12 wks
Sofosbuvir + RBV 16 wks

SVR12 (%)

No Cirrhosis
Cirrhosis

n/N =

VALENCE
SOF + RBV in IFN-naïve and IFN-experienced Patients With GT 3 HCV

• Phase III study

ALLY-3

All-oral 12-week Combination Treatment with DCV + SOF in HCV GT 3

Efficacy and safety of daclatasvir (DCV) + SOF for 12 weeks in GT 3 TN or TE

<table>
<thead>
<tr>
<th>Wk 0</th>
<th>Wk 12</th>
<th>Wk 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV 60 mg + SOF 400 mg QD (n = 101)</td>
<td>SVR&lt;sub&gt;12&lt;/sub&gt;</td>
<td>SVR&lt;sub&gt;12&lt;/sub&gt;</td>
</tr>
<tr>
<td>DCV 60 mg + SOF 400 mg QD (n = 51)</td>
<td></td>
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</tr>
</tbody>
</table>

### Treatment-naïve

<table>
<thead>
<tr>
<th>Treatment-naïve</th>
<th>n = 101</th>
<th>Treatment-experienced&lt;sup&gt;a&lt;/sup&gt;</th>
<th>n = 51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>53 (24-67)</td>
<td>58 (40-73)</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>58 (57)</td>
<td>32 (63)</td>
<td></td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>92 (91)</td>
<td>45 (88)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>4 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>HCV RNA ≥ 800 IU/mL, n (%)</td>
<td>70 (69)</td>
<td>38 (75)</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>19 (19)</td>
<td>13 (25)</td>
<td></td>
</tr>
<tr>
<td>IL28B non-CC genotype, n (%)</td>
<td>61 (60)</td>
<td>31 (61)</td>
<td></td>
</tr>
<tr>
<td>Prior treatment failure, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>-</td>
<td>31 (61)</td>
<td></td>
</tr>
<tr>
<td>Null response</td>
<td>-</td>
<td>7 (14)</td>
<td></td>
</tr>
<tr>
<td>Partial response</td>
<td>-</td>
<td>2 (4)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Patients who previously failed treatment with SOF (n = 7) or alisporivir (n = 2) were included

ALLY-3
DCV + SOF x 12 weeks in HCV GT 3
SVR$_{12}$ Results

Overall SVR$_{12}$

<table>
<thead>
<tr>
<th>Treatment-naïve</th>
<th>91/101</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR$_{12}$ (%)</td>
<td>90</td>
</tr>
</tbody>
</table>

SVR$_{12}$ in Patients With and Without Cirrhosis

<table>
<thead>
<tr>
<th>Cirrhosis Status</th>
<th>73/75</th>
<th>11/19</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR$_{12}$ (%)</td>
<td>97</td>
<td>58</td>
</tr>
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</table>

ELECTRON-2
Sofosbuvir-Ledipasvir ± Ribavirin in GT 1 & 3

Cross-Study Comparison: VALENCE, ELECTRON-2, ALLY-3, and PROTON/ELECTRON

Regimens for HCV GT 3: Treatment-naïve

Similar SVR$_{12}$ rates in TN HCV GT 3; response in cirrhotics still not optimal.

• Patients with GT 3 CHC infection, in combination with RBV:
  - A fibrosis stage of F2, F3, or F4
  - Previous treatment experience with PegIFN/RBV or a medical contraindication to PegIFN/RBV
  - 24 weeks

• Other therapies in Canada:
  - SOF/LDV: no Health Canada indication
  - Daclatasvir…
    - Approved in Europe and Japan
    - EASL Guidelines: option for GT 3: 12 weeks SOF + DCV in naïve patients
Case 2: Cirrhotic Treatment-experienced

- 54M with GT 3 HCV
- 2007: Biopsy proven cirrhosis
  - PegIFN and ribavirin 800 mg for 24 weeks
  - No on-treatment assessment of virologic response; EOT negative
  - Relapsed
- 2011: Retreated PegIFN and weight-based ribavirin 1,400 mg;
  - Week 4 RNA neg, completed 24 weeks
  - Relapsed
- Stable, normal synthetic function
  - What now?
VALENCE
SOF + RBV in IFN-naïve and IFN-experienced Patients With GT 3 HCV

• Phase III study

LONESTAR-2
PegIFN/RBV + SOF x 12 Wks in GT 2 or GT 3 Patients (Phase II)

Open-label Study of Sofosbuvir + RBV With or Without PegIFN Alfa-2a in GT 2 or 3 CHC

• GT 3 mono-infected subjects, including cirrhosis
  • Treatment-naïve
  • Treatment failures

• GT 2 cirrhotic treatment failure

• Subjects randomized to 1:1:1 to 3 arms:
  • SOF + RBV x 16 weeks
  • SOF + RBV x 24 weeks
  • P + R + SOF x 12 weeks
ALLY-3
All-Oral 12-week Combination Treatment with DCV+SOF in HCV GT 3

Efficacy and safety of daclatasvir (DCV) + SOF for 12 weeks in GT 3 TN or TE

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* Patients who previously failed treatment with SOF (n = 7) or alisporivir (n = 2) were included

ALLY-3

DCV + SOF x 12 weeks in HCV GT 3

SVR$_{12}$ Results

Overall SVR$_{12}$

- Treatment-naïve: 90%
- Treatment-experienced: 86%

SVR$_{12}$ in Patients With and Without Cirrhosis

- Non-Cirrhotic: 97%
- Cirrhotic: 58%
- Treatment-naïve: 73/75
- Treatment-experienced: 32/34

- Non-Cirrhotic: 94%
- Cirrhotic: 69%
- Treatment-naïve: 9/13
- Treatment-experienced: 11/19

## ALLY-3

### Safety and Tolerability of SOF + DCV x 12 Wks in GT 3 HCV Patients

<table>
<thead>
<tr>
<th>Parameter, n (%)*</th>
<th>All Patients (N = 152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>1 (1)†</td>
</tr>
<tr>
<td>AEs leading to discontinuation</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3/4 AEs</td>
<td>3 (2)‡/0</td>
</tr>
<tr>
<td>AEs in ≥ 10% of patients (all grades)</td>
<td></td>
</tr>
<tr>
<td>▪ Headache</td>
<td>30 (20)</td>
</tr>
<tr>
<td>▪ Fatigue</td>
<td>29 (19)</td>
</tr>
<tr>
<td>▪ Nausea</td>
<td>18 (12)</td>
</tr>
<tr>
<td>Grade 3/4 laboratory abnormalities</td>
<td></td>
</tr>
<tr>
<td>▪ Hemoglobin &lt; 9.0 g/dL</td>
<td>0</td>
</tr>
<tr>
<td>▪ Absolute lymphocytes &lt; 0.5 x 10⁹/L</td>
<td>1 (1)</td>
</tr>
<tr>
<td>▪ Platelets &lt; 50 x 10⁹/L</td>
<td>2 (1)</td>
</tr>
<tr>
<td>▪ International normalized ratio &gt; 2 x ULN</td>
<td>2 (1)</td>
</tr>
<tr>
<td>▪ Lipase &gt; 3 x ULN</td>
<td>3 (2)</td>
</tr>
</tbody>
</table>

*On-treatment events for death and AEs; treatment-emergent events for grade 3/4 laboratory abnormalities.

†1 event of gastrointestinal hemorrhage at Wk 2, considered not related to study treatment.

‡Arthralgia in 1 patient; food poisoning, nausea, and vomiting in 1 patient; and serious AE of gastrointestinal hemorrhage in 1 patient.

SOF/LDV ± RBV x 12 Wks in Treatment-naïve and Experienced Patients With GT 3 or 6 HCV

- Non-randomized, open-label Phase III trial
- Primary endpoint: SVR\textsubscript{12}
- Cirrhosis present in 44% of GT 3 patients and 8% of GT 6 patients

**Efficacy of SOF/LDV ± RBV x 12 Wks in Patients With GT 3 or 6 HCV**

<table>
<thead>
<tr>
<th>SVR(_{12}), % (n/N)</th>
<th>GT 3 Tx-experienced Patients</th>
<th>GT 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>82 (41/50)</td>
<td>96 (24/25)</td>
</tr>
<tr>
<td>By cirrhosis status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cirrhosis</td>
<td>89 (25/28)</td>
<td>NR</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>73 (16/22)</td>
<td>NR</td>
</tr>
</tbody>
</table>

- GT 3 HCV remains difficult to treat, particularly in treatment-experienced cirrhotic patients

Cross-Study Comparison: VALENCE, ELECTRON-2, ALLY-3, and LONESTAR-2 Regimens for HCV GT 3: Treatment-experienced

Similar SVR\(_{12}\) rates in TE HCV GT 3 non-cirrhotic; Peg/RBV/SOF may be better in TE cirrhotics (await BOSON)

Case 3: Post-transplant

- 58M HCV GT 3 and ESRD due to polycystic kidney disease
- 2009
  - Liver biopsy F2 fibrosis
  - Treated pegIFN and reduced dose ribavirin; relapsed
- 2010
  - Deceased donor renal transplant; uncomplicated, CR ~ 85 mmol/L
  - Tacrolimus, mycophenolate sodium and prednisone 2.5 mg every other day
- Progressive rise in liver stiffness to 15.5 kPa April 2014 and 21.5 March 2015 with mild splenomegaly, platelets 120, albumin 35
HCV Post-SOT

- HCV progression accelerated post transplant
  - Liver: 20%-25% cirrhosis by 5 years
  - Renal: Increased risk of death from liver disease at 10 years (survival 66% vs. 80%)

- Increased risk of extrahepatic complications
  - Post-transplant diabetes
  - Recurrent or *de novo* glomerulonephritis
  - Coronary vasculopathy (heart transplant)
  - May increase risk of PTLD

Northup et al. Transpl Int. 2010.
Interferon-free Therapy: A “Game-changer” Pre- and Post-transplant

• Pre-transplant
  • Liver: IFN-based therapy contraindicated in decompensated; poor response and tolerability even in compensated
  • Non-hepatic: Ribavirin relatively contraindicated in ESRD; IFN-based therapy poorly tolerated in ESRD, advanced lung disease, and contraindicated in severe cardiac disease

• Post-transplant
  • Liver: Low SVR, poor tolerability of IFN-based therapy; HCV recurrence the most significant factor impacting outcomes
  • Non-hepatic: IFN contraindicated due to risk of IFN-induced rejection
Safety and Efficacy Of New DAA-based Therapy for Hepatitis C Post-transplant: Interval Results from HCV-TARGET

- Prospective observational (US, Germany, Canada)
- N = 237
  - Peg/RBV/SOF: 30 SIM/SOF: 117
  - SOF/RBV: 58 SIM/SOF/RBV: 32
- GT 1 SIM/SOF ± RBV: 68 evaluable, 90% SVR4
  - 86% cirrhotics vs. 94% non-cirrhotics
  - 83% 1a vs. 95% 1b
  - 77% MELD > 10 vs. 92% ≤ 10
- Peg/RBV/SOF SVR 83% (GT 1); 100% (GT 3)
- SOF/RBV SVR 90% (GT 2); 60% (GT 3)

SOLAR-1
LDV/SOF + RBV for Treatment of HCV in Patients with Post-transplant Recurrence

Prospective, multicenter study in TN and TE HCV GT 1 and 4 patients, who were post-liver transplantation received 12 or 24 weeks of LDV/SOF + RBV*

*RBV dosing: F0–F3 and CTP A cirrhosis: weight-based (< 75 kg = 1,000 mg; ≥ 75 kg = 1,200 mg); CTP B and C cirrhosis: dose escalation, 600 mg-1,200 mg/d

High rate of SVR₁₂ irrespective of disease severity or duration of therapy

Error bars represent 2-sided 90% exact confidence intervals. 8 CTP B 24-week and 1 CTP C 24-week subjects have not reached the Week 12 post treatment visit.

Efficacy of DAA Combos in GT 1 Liver Transplant Recipients without Cirrhosis


*Mostly GT 1
High Efficacy and Favorable Safety Profile of Daclatasvir-based All-oral Antiviral Therapy in Liver Transplant Recipients with Severe Recurrent HCV

<table>
<thead>
<tr>
<th>HCV RNA Level, n (%)</th>
<th>Baseline (N = 30)</th>
<th>EOT (n = 24)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>≥ 12 Weeks After EOT (n = 12)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undetectable</td>
<td>1 (3)</td>
<td>19 (79)</td>
<td>9 (75)</td>
</tr>
<tr>
<td>Detectable, but &lt; 43 IU/mL</td>
<td>0</td>
<td>5 (21)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>43 to &lt; 999 IU/mL</td>
<td>2 (7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>999 to &lt; 1,000,000 IU/mL</td>
<td>12 (40)</td>
<td>0</td>
<td>1 (8)</td>
</tr>
<tr>
<td>≥ 1,000,000 IU/mL</td>
<td>15 (50)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

EOT, end of treatment

<sup>a</sup> 6 patients died during treatment

<sup>b</sup> 12 patients did not have sufficient follow-up at the time of data collection

Fontana et al AASLD 2014 LB22.
## Studies on PK/PD in Patients With Renal and Hepatic Impairment

<table>
<thead>
<tr>
<th>DAA</th>
<th>Primary Metabolic Pathway</th>
<th>Suitable in Patients With Cirrhosis</th>
<th>Suitable if Renal Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CTP-A</td>
<td>CTP-B</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Renal</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td>Hepatic</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Hepatic</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

SOF Renal Insufficiency Study

SOF + RBV in Patients with Severe Renal Impairment

- Similar rapid virologic decline observed to those with normal renal function
- SVR$_{4}$ and SVR$_{12}$: 40%

**SOF and GS-331007 Pharmacokinetics**

<table>
<thead>
<tr>
<th></th>
<th>SOF (200 mg)</th>
<th>GS-331007 (400 mg)</th>
<th>SOF (400 mg)</th>
<th>GS-331007 (200 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF AUC (ng·h/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GS-331007 AUC (ng·h/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dots indicate patients with SVR4 (blue dots) or viral relapse (red dots).

- Comparable SOF and ~ 4-fold higher GS-331007 exposures compared with historical HCV-infected population

**Adverse Events**

<table>
<thead>
<tr>
<th></th>
<th>SOF 200 mg + RBV N = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>5</td>
</tr>
<tr>
<td>Headache</td>
<td>4</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3</td>
</tr>
<tr>
<td>Rash</td>
<td>3</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>2</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>2</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2</td>
</tr>
<tr>
<td>Irritability</td>
<td>2</td>
</tr>
</tbody>
</table>

- Mean eGFR change from baseline to EOT (Week 24): -3.12 mL/min
- No treatment-emergent clinically significant ECG results

SOF 200 mg + RBV was safe and relatively well-tolerated in patients with severe renal impairment with exacerbation of anemia via RBV-induced hemolysis as primary AE

Gane, AASLD, 2014, Poster #966.
Opportunities to Treat HCV in Non-Hepatic SOT Patients

Pre-transplant Antiviral Therapy

No currently approved therapies

Post-transplant Antiviral Therapy

GT 3
- SOF/RBV
- SOF/DCV ± RBV
- ?? SOF/LDV ± RBV

GT 1
- SOF/LDV + RBV
- OBV + PTV/r + DSB + RBV
- SIM/SOF ± RBV
What Is Next in GT 3 HCV?
SVR\textsubscript{12} With SOF + GS-5816: 12 Wks Effective in GT 1, 2, and 3

**SOF + GS-5816 ± RBV x 8 Wks in Non-cirrhotic Patients With GT 3 HCV**

- Randomized, open-label Phase II trial
- Primary endpoint: SVR$_{12}$

Treatment-naïve non-cirrhotic patients with GT 3 HCV (N = 104)

- SOF + GS-5816 25 mg QD (n = 27)
- SOF + GS-5816 25 mg QD + RBV (n = 24)
- SOF + GS-5816 100 mg QD (n = 27)
- SOF + GS-5816 100 mg QD + RBV (n = 26)

Patients followed to Wk 20

SVR\textsubscript{12} With SOF + GS-5816 ± RBV x 8 Wks in Non-cirrhotic GT 3 Patients

<table>
<thead>
<tr>
<th>SVR\textsubscript{12}, % (n/N)</th>
<th>GT 3 Non-cirrhotic Patients</th>
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<tr>
<td></td>
<td>SOF + GS-5816 25 mg (n = 27)</td>
</tr>
<tr>
<td>Overall</td>
<td>100</td>
</tr>
</tbody>
</table>

- Baseline NS5A RAVs had no effect on efficacy

• Safety and Efficacy Study of Daclatasvir 60 mg, Sofosbuvir 400 mg, and Ribavirin (Dosed Based Upon Weight) in Subjects With Chronic Genotype 3 Hepatitis C Infection With or Without Prior Treatment Experience and Compensated Advanced Cirrhosis for 12 or 16 Weeks (recruiting NCT02319031)

• Study to Evaluate the Safety and Efficacy of Daclatasvir/Sofosbuvir/Ribavirin for 16 Versus 24 Weeks for HCV Genotype 3 Cirrhotics (recruiting NCT02304159)
  • This is a randomized, open label, single center safety and efficacy study. At least 40 cirrhotic subjects with HCV GT 3 will receive standard of care treatment of sofosbuvir and ribavirin (SOF/RBV) as well as 60 mg daily of daclatasvir (investigational product). Subjects will be randomized in a 1:1 to receive either:
    • Group A: 16 weeks of DCV/SOF/RBV
    • Group B: 24 weeks of DCV/SOF/RBV
Conclusions

• GT 3 HCV is the most difficult to cure in 2015
  • Particularly those with cirrhosis and prior treatment failure
• PegIFN-based therapy remains the backbone of therapy for many
  • Public funding
  • In treatment-experienced cirrhotics, this may be the best therapy
• On the horizon:
  • SOF/GS-5816/RBV
  • SOF/DCV/RBV
• Paradigm shift of HCV therapy in organ transplantation
  • Renal failure remains a contraindication to SOF-based therapy
  • ?Use of HCV-infected donors
Questions?
ALLY-2
SOF + DCV in GT 1-6 HCV/HIV-Coinfected Patients

- Phase III open-label study
- Non GT 1 < 20% in each cohort; compensated cirrhosis < 50% overall; HIV-1 RNA < 50 c/mL and CD4+ ≥ 100 in patients on ART; CD4 ≥ 350 in patients not on ART
- ART allowed: PI/RTV, NRTIs, NNRTIs, INSTIs, MVC, ENF
- Primary endpoint: SVR_{12} in GT 1 naïve patients treated for 12 wks

*Standard dose of 60 mg adjusted for ART: 30 mg with RTV; 90 mg with NNRTIs except RPV.

ALLY-2
Virologic Outcomes With SOF + DCV in HIV/HCV-Coinfected Patients

- High SVR$_{12}$ rates with 12 wks SOF + DCV
- Large decline in SVR rate with shortening to 8 wks

- In 12-wk groups analyzed by GT, 100% with SVR$_{12}$ except GT 1a
  - GT 1a-naïve: 96%; experienced: 97%

- Similar SVR$_{12}$ rates in patients with or without baseline NS5A RAVs

- 12 patients with relapse, 10 in 8-wk arm
  - 1 in 8-wk arm had emergent NS5A RAVs

- No NS5B RAVs at BL or time of failure

- No discontinuation of therapy due to AEs

- 10 patients with HIV-1 RNA > 50 at EOT
  - 8 with repeat testing; 7 with suppression without change in ART; 1 with HIV-1 RNA of 59; 2 LTFU

- 2 with HIV VF = HIV-1 RNA ≥ 400 c/mL

PHOTON-1
Sofosbuvir + RBV in GT 1-3 HCV Patients Coinfected With HIV

- Non-randomized, open-label Phase III study; primary endpoint: SVR$_{12}$
- Stable ART (HIV-1 RNA < 50 copies/mL for > 8 wks before enrollment)
- 95% on ART: TDF/FTC, 100%; EFV, 35%; ATV/RTV, 17%; DRV/RTV, 15%; RAL, 16%; RPV, 6%
- Cirrhosis at baseline: GT 1, 4%; GT 2/3 Tx-naïve, 10%; GT 2/3 Tx-experienced: 24%

Sofosbuvir 400 mg QD; weight-based RBV 1,000 or 1,200 mg/day

PHOTON-2
Sofosbuvir + RBV in GT 1-4 HCV Patients Coinfected With HIV

- Non-randomized, open-label Phase III study; primary endpoint: SVR_{12}
- Stable ART (HIV-1 RNA < 50 copies/mL for ≥ 8 wks before enrollment)
- 97% on ART: TDF/FTC, 100%; EFV, 25%; ATV/RTV, 17%; DRV/RTV, 21%; RAL; 23%; RPV, 5%
- Cirrhosis at baseline: All patients, 20%; Tx-naïve patients, 13%; Tx-experienced patients, 45%

Sofosbuvir 400 mg QD; weight-based RBV 1,000 or 1,200 mg/day
**PHOTON-2**

**SVR\textsubscript{12} by GT and Cirrhosis**

- Absolute CD4+ count—but not CD4%—decreased, consistent with effect of RBV on lymphocytes