Hepatitis C Post-OLT
Who, What, When?

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Disclosures

- Grant Support/Consultant for Abbvie, BMS, Genentech, Gilead, Janssen, Merck, Vertex
Recurrent HCV Infection Post-LT

When to treat?

- **Cirrhosis**
- **Transplant**
- **Normal histology**

**Pre-LT**

- Prevent recurrent HCV

**Preemptive**

- 0 weeks
- 4-6 weeks

**Acute hepatitis**

**PHOENIX study** showed no benefit with PEG+RBV. No studies of new DAA in this setting.

**Prevent recurrent HCV**
When/Who to Treat

• Will all patients be HCV RNA (-) going into OLT?
  – HCC upgrades, LDLT-Possible
  – Patients treated earlier with SVR who develop HCC
  – Decompensated, high MELD-Not at the current time, ? Soon

• Will decrease risk of early recurrence but may have decreased response and access to HCV + livers
Phase 3
Open-label
Genotype 1
Treatment-naïve and
PR experienced
Child-Pugh A
Platelets: ≥60K/mL
Serum albumin: >2.8 g/dL
Total bilirubin: <3 g/dL
INR: <2.3
AFP: ≤100 ng/mL

Week 0 12 24

ABT-450/r/Ombitasvir + Dasabuvir + RBV (n=208)

ABT-450/r/Ombitasvir + Dasabuvir + RBV (n=172)

ABT-450/ritonavir/ombitasvir 150/100/25 mg qd; dasabuvir 250 mg bid. RBV (1000-1200 mg). PR: pegIFN + RBV.
Primary endpoint: SVR12 versus historical control SVR rate: 43% and 54% for non-inferiority and superiority, respectively (telaprevir + PR).
Baseline demographics and disease characteristics:
- Male: 70%; age: 57 years; black: 4%-6%.
- Genotype 1a: 67%-70%.
- IL28B non-CC: 80%-83%.
- Treatment naïve: 41%-43%.
- Prior PR response:
  - Relapse: 13%-14%.
  - Partial response: 8%-9%.
  - Null response: 36%.
- Child-Pugh score >5: 18%-19%.

TURQUOISE-II: SVR12 Rates With ABT-450/r/Ombitasvir + Dasabuvir + RBV in HCV Genotype 1, Compensated Cirrhotics


PR: pegIFN + RBV.

Pre-LT Antiviral Therapy with Sofosbuvir + Ribavirin

- Single-arm, open-label phase II study from 16 liver transplantation sites
  - HCC with MELD upgrades

- Excluded:
  - LDLT
  - Decompensated cirrhosis (CTP >8)
  - Renal impairment (CrCl <60 cc/min)

- Pre-LT therapy for 48 weeks or until LT:
  - Sofosbuvir 400 mg/day
  - Ribavirin 1000-1200 mg/day

- Post-LT immunosuppression:
  - Tacrolimus (≥12 weeks)
  - Prednisone
  - MMF

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SOF + RBV (N = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yrs (range)</td>
<td>59 (46-73)</td>
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<tr>
<td>HCV genotype, %</td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>39</td>
</tr>
<tr>
<td>1b</td>
<td>34</td>
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<tr>
<td>2</td>
<td>13</td>
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<tr>
<td>3a</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Non-CC IL28B genotype, %</td>
<td>78</td>
</tr>
<tr>
<td>CTP score, %</td>
<td></td>
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<tr>
<td>5-7</td>
<td>96</td>
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<tr>
<td>8</td>
<td>5</td>
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<tr>
<td>Previous HCV treatment, %</td>
<td>75</td>
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Pre-LT Sofosbuvir + Ribavirin to Prevent Post-LT HCV Recurrence

- 61 pts enrolled in study;
  - 67% (41/61) received LT with HCV RNA <25 IU/mL
  - 91% (30/33) who received ≥12 wks therapy had HCV RNA <25 IU/mL at time of LT

- HCV RNA decreased rapidly
  - Mean 4.5 log units after 2 weeks of therapy

- 64% (25/39) of evaluable pts had HCV RNA negative 12 wks post-LT

Duration of Undetectable HCV RNA Before Transplant Predicted Lack of Recurrence

- Continuous days of undetectable HCV RNA pre-LT only factor predicting HCV recurrence in multivariate analysis
- Median days TND (p<0.001)
  - No recurrence 95 days
  - Recurrence 5.5 days

Ledipasvir/Sofosbuvir + RBV in HCV Genotype 1 or 4 with Decompensated Cirrhosis

Phase 2
Open-label
Genotype 1 or 4
CPT class B or C
Treatment-naïve or experienced
No organ transplantation or HCC
Total bilirubin <10 mg/dL
Hemoglobin >10 g/dL
CrCl: >40 mL/min
Platelets: >30K x 10³/µL

Ledipasvir/Sofosbuvir qd + RBV (n=53)

Ledipasvir/Sofosbuvir qd (n=55)

Week 0 12 24

CPT: Child-Pugh-Turcotte.
PR: pegIFN + RBV.
Ledipasvir/sofosbuvir 90/400 mg qd + weight-based RBV(1000-1200 mg).
Primary endpoint: SVR12.
Baseline demographics:
Male: 61%-73%.
Mean age: 58-60 years
White: 90%-97%
Genotype 1a: 63%-76%.
HCV RNA (log₁₀ IU/mL): 5.6-5.9.
IL28B non-CC: 73%-87%.
BMI >30 kg.m²: 33%-57%.

Ledipasvir/Sofosbuvir + RBV in HCV Genotype 1 or 4: Baseline Liver Status

<table>
<thead>
<tr>
<th></th>
<th>CPT B (n=30)</th>
<th>24 Weeks (n=29)</th>
<th>CPT C (n=23)</th>
<th>24 Weeks (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MELD score (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
<td>20</td>
<td>28</td>
<td>0</td>
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<tr>
<td>10-15</td>
<td>70</td>
<td>55</td>
<td>70</td>
<td>50</td>
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<tr>
<td>16-20</td>
<td>10</td>
<td>17</td>
<td>30</td>
<td>46</td>
</tr>
<tr>
<td>21-25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Ascites (%)</td>
<td>57</td>
<td>59</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Encephalopathy (%)</td>
<td>67</td>
<td>55</td>
<td>91</td>
<td>88</td>
</tr>
<tr>
<td>Median bilirubin (mg/dL)</td>
<td>2.0</td>
<td>1.4</td>
<td>2.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Median albumin (g/dL)</td>
<td>2.9</td>
<td>3.0</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Median INR</td>
<td>1.3</td>
<td>1.3</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Median platelets (x 10^3/μL)</td>
<td>88</td>
<td>73</td>
<td>81</td>
<td>71</td>
</tr>
<tr>
<td>Median hemoglobin (g/dL)</td>
<td>13.1</td>
<td>13</td>
<td>12.3</td>
<td>12.6</td>
</tr>
<tr>
<td>Median creatinine clearance (mL/min)</td>
<td>98</td>
<td>81</td>
<td>77</td>
<td>78</td>
</tr>
</tbody>
</table>

CPT: Child-Pugh-Turcotte.

Ledipasvir/Sofosbuvir + RBV in HCV Genotype 1 or 4: Preliminary Results

- High SVR12 rates in HCV patients with advanced liver disease
- CPT B and C patients at post-treatment week 4
  - Significant improvements in median total bilirubin and albumin
  - Change in CPT scores
    - Improved: 70%
    - Stable: 21%
    - Worsened: 9%
  - Change in MELD score (CPT B/C)
    - Improved: 64%/70%
    - Stable: 19%/13%
    - Worsened: 17%/18%

# Ledipasvir/Sofosbuvir + RBV in HCV Genotype 1 or 4: Preliminary Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>CPT B</th>
<th>CPT C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 Weeks (n=30)</td>
<td>24 Weeks (n=29)</td>
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<tr>
<td>Grade 3/4 adverse events (%)</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Serious adverse events (%)</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td>Treatment-related serious adverse event (%)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Treatment discontinuations due to adverse events (%)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

CPT: Child-Pugh-Turcotte.
Treatment-related serious adverse events: anemia (n=2), hepatic encephalopathy (n=1), peritoneal hemorrhage (n=1).
Early discontinuations (n=1 for each): sepsis, hepatic encephalopathy, peritoneal hemorrhage.
Deaths: septic shock (n=2), multi-organ failure and shock (n=2), oliguric renal failure (n=1), cardiac arrest (n=1).

When/Who to Treat

- Pre-emptive/prophylactic post-OLT is ideal, but...
  - No clear established regimen or duration
  - Higher levels of immunosuppression
  - Off-label
  - IMS and liver function is changing, DDI’s will be more difficult and toxicity difficult to interpret (DILI, rejection, etc)
  - What is benefit vs waiting until stable?
When/Who to Treat

• Reactive post-OLT is current standard for most
  – Graft stabilized but VL higher
  – IMS lower and stable
  – Identifies those who can wait for better Rx or maybe do not need Rx?
  – Histologic trigger may be milder as therapies improve--F2 any time? Any fibrosis in 1st year(s)?, ALT or grade on bx?

• As treatments improve earlier, universal Rx likely to be the rule
Sofosbuvir + RBV for Treatment of Post-LT HCV Recurrence

- Prospective, multicenter, single-arm, open-label pilot study
  - CTP ≤ 7 and MELD ≤ 17
  - 40% with compensated cirrhosis

- Treatment:
  - SOF 400 mg/day
  - RBV 400-1200 mg/day for ≤ 24 wks
  - RBV started at 400 mg/day and increased based on hemoglobin levels

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SOF+RBV (N=40)</th>
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<tbody>
<tr>
<td>Median Age, yrs (range)</td>
<td>59 (49-75)</td>
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<tr>
<td>Male, %</td>
<td>78</td>
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<tr>
<td>White, %</td>
<td>85</td>
</tr>
<tr>
<td>Mean time from LT, yrs (range)</td>
<td>4.3 (1.02-10.6)</td>
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<tr>
<td>HCV genotype, %</td>
<td></td>
</tr>
<tr>
<td>- 1a</td>
<td>55</td>
</tr>
<tr>
<td>- 1b</td>
<td>28</td>
</tr>
<tr>
<td>- 2</td>
<td>0</td>
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<tr>
<td>- 3</td>
<td>15</td>
</tr>
<tr>
<td>- 4</td>
<td>3</td>
</tr>
<tr>
<td>Non-CC IL28B genotype, %</td>
<td>67%</td>
</tr>
<tr>
<td>Mean HCV RNA, log_{10} IU/mL (range)</td>
<td>6.55 (4.49-7.59)</td>
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<tr>
<td>Previous HCV treatment, %</td>
<td>88</td>
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<tr>
<td>Fibrosis stage (F3-F4), %</td>
<td>63</td>
</tr>
</tbody>
</table>
Baseline characteristics similar in patients with and without virologic relapse
Sofosbuvir + RBV for Post-LT HCV Recurrence: Safety Outcomes

- No deaths, graft loss, or rejection
- No drug–drug interactions with immunosuppressive agents
- RBV dose reduction in 28%; 20% received epoetin and/or blood products


Real-World Use of Sofosbuvir-Based Regimens in Recurrent HCV Post-Liver Transplantation: HCV TARGET Study

- Ongoing longitudinal, observational study of DAA-based therapy in recurrent HCV post-liver transplant (n=245)
  - 38 academic and 15 community medical centers in the US, Germany, and Canada
  - HCV treatment is administered according local standard of care
    - Regimen selection made by health care provider
- Interim results for sequentially enrolled patients who started therapy with sofosbuvir-containing regimens
  - Genotype 1 (n=179): sofosbuvir + simeprevir + RBV (79.7%), sofosbuvir + PR (13.4%), sofosbuvir + RBV (7.3%)
  - Genotype 2 (n=20): sofosbuvir + RBV (100%)
  - Genotype 3 (n=19): sofosbuvir + RBV (94.7%), sofosbuvir + PR (5.3%): PR: pegIFN + RBV.


<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Patients (n=227)</th>
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<tbody>
<tr>
<td>Male (%)</td>
<td>73.6</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>60.0</td>
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<tr>
<td>&gt;65 years (%)</td>
<td>19.8</td>
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<td>Black (%)</td>
<td>8.4</td>
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<tr>
<td>Treatment experienced (%)</td>
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<tr>
<td>Naïve</td>
<td>42.7</td>
</tr>
<tr>
<td>Experienced</td>
<td>57.3</td>
</tr>
<tr>
<td>PI failure</td>
<td>11.5</td>
</tr>
<tr>
<td>Circrhosis (%)</td>
<td>56.4</td>
</tr>
<tr>
<td>MELD &gt;10 (%)</td>
<td>31.3</td>
</tr>
<tr>
<td>Immunosuppression (%)</td>
<td></td>
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<tr>
<td>TAC</td>
<td>76.7</td>
</tr>
<tr>
<td>CSA</td>
<td>12.3</td>
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<tr>
<td>Everolimus/sirolimus</td>
<td>15.9</td>
</tr>
<tr>
<td>MMF/MPA</td>
<td>42.3</td>
</tr>
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HCV TARGET Study (Interim Results): Crude SVR4 Rates With Sofosbuvir + Simeprevir ± RBV in Recurrent HCV Post-Liver Transplantation

**HCV Genotype 1**

<table>
<thead>
<tr>
<th>SVR4 Rate (%)</th>
<th>SOF SIM</th>
<th>SOF SIM</th>
<th>Yes (n=37)</th>
<th>No (n=31)</th>
<th>Yes (n=37)</th>
<th>No (n=31)</th>
<th>&lt;10 (n=12)</th>
<th>&gt;10 (n=13)</th>
<th>1a (n=36)</th>
<th>1b (n=19)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>RBV (n=11)</td>
<td>-- (n=57)</td>
<td>Cirrhosis</td>
<td>Treatment Experienced</td>
<td>MELD</td>
<td>Genotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir + Simeprevir</td>
<td>No RBV</td>
<td>With RBV</td>
<td>82%</td>
<td>91%</td>
<td>86%</td>
<td>94%</td>
<td>89%</td>
<td>90%</td>
<td>92%</td>
<td>77%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(n=37)</td>
<td>(n=31)</td>
<td>(n=37)</td>
<td>(n=31)</td>
<td>(n=12)</td>
<td>(n=13)</td>
<td>(n=36)</td>
<td>(n=19)</td>
</tr>
</tbody>
</table>

HCV TARGET Study (Interim Results): Treatment Outcomes With Sofosbuvir + Simeprevir + RBV in Recurrent HCV Post-Liver Transplantation

- Additional SVR4 rates
  - Sofosbuvir + PR: 83% (10/12 genotype 1); 100% (1/1 genotype 3)
  - Sofosbuvir + RBV: 90% (9/10 genotype 2), 60% (3/5 genotype 3)

- Predictors of SVR4 (adjusted for cirrhosis status, previous treatment, prior decompensation)
  - For: baseline hemoglobin, age
  - Against: baseline total bilirubin

- Safety
  - ≥1 adverse event (82%, most deemed mild in severity)
  - Discontinuations due to adverse events (2.2%)
  - Serious adverse events (8.5%)
  - No episodes of acute cellular rejection
  - Renal failure (n=3; sofosbuvir + simeprevir [2], sofosbuvir + simeprevir + RBV [1])

PR: pegIFN + RBV.

Ledipasvir/Sofosbuvir + RBV for Post-Transplantation HCV Recurrence (Genotype 1 or 4)

Phase 2

Open-label
Genotype 1 or 4
CPT class A, B, or C
Treatment-naïve or experienced
No HCC
Total bilirubin ≤10 mg/dL
Hemoglobin ≥10 g/dL
CrCl: >40 mL/min
Platelets: >30K x 10³/µL

Ledipasvir/Sofosbuvir qd + RBV (n=112)

Ledipasvir/Sofosbuvir qd + RBV (n=111)

Week 0 12 24

CPT: Child-Pugh-Turcotte.
Ledipasvir/sofosbuvir 90/400 mg qd.
RBV (F0-F3 and CPT A cirrhosis: weight based; CBT B and C: continuous dose escalation 600-1200 mg).
Primary endpoint: SVR12.
Baseline demographics:
  Male: 80%-100%.
  Mean age: 59-61 years
  White: 80%-89%
  Genotype 1a: 67%-78%
  HCV RNA (log₁₀ IU/mL): 6.3-6.6.
  IL28B non-CC: 67%-85%
  Median time from orthotopic liver transplantation: 2.9-8.1 years
  Prior HCV treatment: 78%-90%.

## Ledipasvir/Sofosbuvir + RBV for Post-Transplantation HCV Recurrence (Genotype 1 or 4): Baseline Liver Status

<table>
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<tr>
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<th>CPT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>F0-F3 (n=111)</td>
<td>A  (n=51)</td>
<td>B  (n=52)</td>
<td>C  (n=9)</td>
</tr>
<tr>
<td>MELD score (%)</td>
<td></td>
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<td></td>
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<tr>
<td>&lt;10</td>
<td>--</td>
<td>55</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>10-15</td>
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<td>63</td>
<td>56</td>
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<td>16-20</td>
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<td>6</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>21-25</td>
<td>--</td>
<td>0</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Ascites (%)</td>
<td></td>
<td>2</td>
<td>4</td>
<td>77</td>
</tr>
<tr>
<td>Encephalopathy (%)</td>
<td></td>
<td>1</td>
<td>6</td>
<td>44</td>
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<tr>
<td>Median bilirubin (mg/dL)</td>
<td></td>
<td>0.7</td>
<td>0.8</td>
<td>1.2</td>
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<tr>
<td>Median albumin (g/dL)</td>
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<td>3.8</td>
<td>3.7</td>
<td>3.2</td>
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<tr>
<td>Median INR</td>
<td></td>
<td>1.0</td>
<td>1.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Median platelets (x 10^3/μL)</td>
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<td>146</td>
<td>108</td>
<td>93</td>
</tr>
<tr>
<td>Median hemoglobin (g/dL)</td>
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<td>14.0</td>
<td>13.6</td>
<td>12.9</td>
</tr>
<tr>
<td>Median creatinine clearance (mL/min)</td>
<td></td>
<td>65</td>
<td>62</td>
<td>59</td>
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</tbody>
</table>

CPT: Child-Pugh-Turcotte.

Preliminary Outcomes: Ledipasvir/Sofosbuvir + RBV for Recurrent HCV Post-Transplantation (HCV Genotype 1 or 4)

- High SVR12 rates in HCV patients with advanced liver disease
- CPT A and B patients at post-treatment week 4
  - Significant improvements in median total bilirubin and albumin
  - Change in MELD score (CPT A/B)
    - Improved: 42%/68%
    - Stable: 27%/12%
    - Worsened: 32%/20%


CPT: Child-Pugh-Turcotte.
Ledipasvir/Sofosbuvir + RBV for Post-Transplantation HCV Recurrence (Genotype 1 or 4): Preliminary Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>F0-F3</th>
<th>CPT A</th>
<th>CPT B</th>
<th>CPT C</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Weeks (n=30)</td>
<td>12 Weeks (n=30)</td>
<td>12 Weeks (n=30)</td>
<td>12 Weeks (n=29)</td>
<td>12 Weeks (n=23)</td>
</tr>
<tr>
<td>24 Weeks (n=29)</td>
<td>24 Weeks (n=29)</td>
<td>24 Weeks (n=29)</td>
<td>24 Weeks (n=29)</td>
<td>24 Weeks (n=26)</td>
</tr>
<tr>
<td>Grade 3/4 adverse events (%)</td>
<td>27</td>
<td>25</td>
<td>28</td>
<td>23</td>
</tr>
<tr>
<td>Serious adverse events (%)</td>
<td>11</td>
<td>21</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>Treatment-related serious adverse event (%)</td>
<td>4</td>
<td>2</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Treatment discontinuations due to adverse events (%)</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Death (%)</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

CPT: Child-Pugh-Turcotte.
Adverse events leading to discontinuation (n-1 for each): shortness of breath, hemoperitoneum, thoracic aorta aneurysm, seizure, elevated ALT/AST, dyspnea.
Treatment-related serious adverse events: anemia (n=4), hemolytic anemia (n=2), portal vein thrombosis (n=1), sick's sinus syndrome (n=1), sinus arrhythmia (n=1).
Treatment emergent deaths (n=1 for each): progressive multifocal leukoencephalitis, thoracic aorta aneurysm, internal bleeding, complications of cirrhosis.

CORAL-I Study: ABT-450/r/Ombitasvir + Dasabuvir + RBV for HCV Genotype 1 After Liver Transplantation

- Ongoing phase 2 study
  - HCV genotype 1 (n=34)
  - Liver transplantation due to HCV infection
    - PR permitted prior to transplantation
    - Treatment-naïve post transplantation
  - METAVIR ≤F2
- On stable immunosuppression
  - Tacrolimus (85%)
  - Cyclosporine (15%)
- Primary outcome: SVR12

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Patients (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>79</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>59.6</td>
</tr>
<tr>
<td>Fibrosis stage (%)</td>
<td></td>
</tr>
<tr>
<td>F0/F1/F2</td>
<td>18/38/44</td>
</tr>
<tr>
<td>Median time since liver transplantation</td>
<td>39.5</td>
</tr>
<tr>
<td>(months)</td>
<td></td>
</tr>
<tr>
<td>Genotype 1a (%)</td>
<td>85</td>
</tr>
<tr>
<td>IL28B non-CC (%)</td>
<td>77</td>
</tr>
<tr>
<td>HCV RNA (log_{10} IU/mL)</td>
<td>6.6</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td>90.5</td>
</tr>
<tr>
<td>ALT/AST (U/L)</td>
<td>78.9/63.9</td>
</tr>
</tbody>
</table>

ABT-450/ritonavir/ombitasvir 150/100/25 mg qd; dasabuvir 250 mg bid. RBV (1000-1200 mg). Tacrolimus: 0.5 mg once weekly or 0.2 mg every 3 days. Cyclosporine: 1/5 of daily dose given once daily prior to HCV therapy.

ABT-450/r/Ombitasvir+Dasavuvir+RBV for Treatment of Recurrent HCV GT1

CORAL-I Study: Treatment Outcomes

- SVR12 and SVR24: 97%
  - No virologic breakthroughs
  - Relapse (n=1)
    - Emergent RAVs at time of relapse: R155K, M28T+Q30R, G554S
- No deaths, graft losses, or episodes of acute or chronic rejection
- Discontinuations due to adverse events (n=1)
- Serious adverse events (n=2)
  - Hypotension and tachycardia associated with tamsulosin
  - Moderate peripheral edema and pain in extremities in a diabetic patient
- All patients who required RBV dose reduction achieved SVR12

ABT-450/r/Ombitasvir+Dasavuvir+RBV for Treatment of Recurrent HCV GT1

- TAC dose 0.5-1.0 mg at 1-2 week intervals for most
- 4 patients had TAC >15 ng/mL, all due to dosing errors

- CsA levels maintained within desired range in all 5 patients
- On treatment CsA dose was 1/5 of pre-treatment dose in these patients

Hepatitis C and Liver Transplantation

- Clearance of HCV post transplant is achievable with either a pre- or post-transplant approach
- DAA’s offer high rates of viral clearance
- Major issues will safety and efficacy in advanced liver disease pre-OLT and DDI post-OLT
- The near-term future offers
  - Early clearance post-OLT with IFN-free, ? Riba free therapy for decompensated disease
  - Pretransplant clearance for LDLT and HCC as well as low MELD waiting list candidates
- Better treatment strategies are needed for CPT C patients particularly if it can stabilize/improve disease