Pan-Genotypic Diret-Acting Antivirals: Opportunity to Achieve HCV Elimination

HEPDART 2017

USA

December 6th, 2017

Tarik Asselah (MD, PhD)
Professor of Medicine
Hepatology, Chief INSERM UMR 1149,
Hôpital Beaujon, Clichy, France.
Disclosures

• Employee of Paris Public University Hospitals (AP-HP, Beaujon’s Hospital) and University of Paris

• Principal investigator for research grants: Funds paid to Hospital (AP-HP)

• Consultant, expert and speaker for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Merck Sharp Dohme, Roche.

• Grants from: ANR, CNRS, INSERM, University of Paris, ANRS
Pan-Genotypic Direct-Acting Antivirals: Opportunity to Achieve HCV Elimination

1. Introduction
2. Sofosbuvir/Velpatasvir (Epclusa®)
3. Glecaprevir/Pibrentasvir (Mavyret®)
4. HCV Elimination
5. Conclusion
Estimated 70 Million Persons Living With HCV

Estimated chronic HCV prevalence, diagnosis rate and treatment rate in 2013

Note: size of bubble depicts viraemic HCV prevalence
SOF + RBV
12–24 weeks

SOF + SMV
± RBV
12–24 weeks

SOF + DCV
± RBV
12–24 weeks

SOF/VEL
± RBV
12 weeks

SOF/VEL/VOX
± DSV ± RBV
12–24 weeks

SOF/LDV
± RBV
8†–24 weeks

OMV/PTV/RTV
± DSV ± RBV
12–24 weeks

GRZ/EBV
± RBV
12–16 weeks

GLE/PIB
8–12 weeks


Asselah, Marcellin & Schinazi. Liver Int 2018, in press.
Pan-Genotypic Direct-Acting Antivirals: Opportunity to Achieve HCV Elimination

1. Introduction

2. Sofosbuvir/Velpatasvir (Epclusa®)

3. Glecaprevir/Pibrentasvir (Mavyret®)

4. HCV Elimination

5. Conclusion
Velpatasvir/Sofosbuvir: A Single Tablet Regimen (STR)

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

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

**SOF/VEL Single Tablet Regimen (STR)**
- Once daily, oral, STR (400/100 mg)

**Sofosbuvir (SOF)/Velpatasvir (VEL)**
- **SOF**: Nucleotide polymerase inhibitor with activity against HCV GT 1–6
- **VEL**: Potent pangenotypic NS5A inhibitor

**Voxilaprevir (VOX)**
- HCV NS3/4A PI with potent antiviral activity against GT 1–6, including most RASs

**SOF/VEL/VOX**
- Once daily, oral, fixed-dose combination (400/100/100 mg) for GT 1–6
Velpatasvir/Sofosbuvir (Epclusa®) for 12 weeks across all genotypes (ASTRAL-1, ASTRAL-2 and ASTRAL-3)

SVR12 (%)

- Total: 98%
  - 1015/1035
- GT 1: 98%
  - 323/328
- GT 2: 99%
  - 237/238
- GT 3: 95%
  - 264/277
- GT 4: 100%
  - 116/116
- GT 5: 97%
  - 34/35
- GT 6: 100%
  - 41/41

- 2% of patients experienced one or more SAE; no SAEs were considered study drug related
- 2 patients discontinued treatment due to AEs

AE: adverse event; D/C: discontinuation; LTFU: lost to follow-up; SAE: serious adverse event

Agarwal K, et al. EASL 2016; Poster #SAT-195;
Jacobson I, et al. EASL 2016; Poster #SAT-168
Velpatasvir/Sofosbuvir (Epclusa®) for 12 weeks in patients with Advanced Fibrosis and Cirrhosis (ASTRAL 1, 2 & 3)

Overall

Advanced fibrosis

Cirrhosis

Patients with SVR (%)

98

99

96

490/501

278/281

212/220

Real-World Experience of SOF/VEL in HCV GT 1–6

HCV-TARGET

407 patients treated with SOF/VEL from the HCV-TARGET registry (patients who started July 2016 - Feb 2017)

Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL n=407</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>228 (56)</td>
</tr>
<tr>
<td>Age ≥60, n (%)</td>
<td>164 (40)</td>
</tr>
<tr>
<td>HCV GT, %</td>
<td></td>
</tr>
<tr>
<td>1 / 2 / 3 / Other</td>
<td>17 / 39 / 38 / 6</td>
</tr>
<tr>
<td>Treatment duration</td>
<td></td>
</tr>
<tr>
<td>12 weeks, n (%)</td>
<td>330 (81)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>39 (10)</td>
</tr>
<tr>
<td>Ongoing</td>
<td>38 (9)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>113 (28)</td>
</tr>
<tr>
<td>History of DC, n (%)</td>
<td>30 (7)</td>
</tr>
<tr>
<td>TE*, n (%)</td>
<td>67 (17)</td>
</tr>
<tr>
<td>Liver transplant, n (%)</td>
<td>8 (2)</td>
</tr>
</tbody>
</table>

* 21 (5%) were DAA treatment failures (per abstract only).

SVR12 for SOF/VEL in this real-world cohort was similar to that reported in registration trials

SVR12 (PP)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>GT 1</th>
<th>GT 2</th>
<th>GT 3</th>
<th>TN</th>
<th>TE</th>
<th>NC</th>
<th>CC</th>
<th>DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12, %</td>
<td>97</td>
<td>94</td>
<td>98</td>
<td>98</td>
<td>99</td>
<td>90</td>
<td>98</td>
<td>94</td>
<td>93</td>
</tr>
</tbody>
</table>

TN=treatment-naïve  
TE=treatment-experienced  
NC=non-cirrhotic  
CC=compensated cirrhotic  
DC=decompensated cirrhotic
SOF/VEL for 12 weeks in patients with recent injecting drug use led to high SVR12 rates despite ongoing drug use.

Efficacy Results (ITT)

<table>
<thead>
<tr>
<th>Response (%)</th>
<th>EOT</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>94%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[
\frac{99}{103} \quad 3 \text{ LTFU} \quad 1 \text{ death}
\]

\[
\frac{97}{103} \quad 4 \text{ LTFU} \quad 1 \text{ death} \quad 1 \text{ RI}
\]

LTFU: loss to follow-up; RI: re-infection
n=4 did not complete treatment (3 LTFU, 1 overdose death)
n=6 did not have an SVR12 (4 LTFU, 1 overdose death, 1 reinfection)
The SVR12 rate was 97% (431/445) in DAA-experienced patients treated with SOF/VEL/VOX for 12 weeks; Rates were similar regardless of genotype

*Patient had drug levels consistent with nonadherence.
Roberts, EASL 2017, SAT-280
Resistance Analysis of SOF/VEL/VOX for 12 Weeks in DAA-Experienced Patients

Integrated Resistance Analysis of POLARIS-1 and -4

Prevalence and Impact on Treatment Outcome of VOX- and VEL-Specific RASs in DAA-Experienced Patients

Drug-specific RASs had no impact on treatment outcome of DAA-experienced patients treated with SOF/VEL/VOX for 12 weeks

Sarrazin, EASL 2017, THU-248
Pan-Genotypic Direct-Acting Antivirals: Opportunity to Achieve HCV Elimination

1. Introduction
2. Sofosbuvir/Velpatasvir (Epclusa®)
3. Glecaprevir/Pibrentasvir (Mavyret®)
4. HCV Elimination
5. Conclusion
Glecaprevir/Pibrentasvir (Mavyret®)

**In vitro:**
- High barrier to resistance
- Potent against common NS3 polymorphisms (e.g., positions 80, 155, and 168) and NS5A polymorphisms (e.g., positions 28, 30, 31, and 93)
- Additive/synergistic antiviral activity

**Clinical PK & metabolism:**
- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

Glecaprevir (ABT-493) is a pangenotypic NS3/4A protease inhibitor and Pibrentasvir (ABT-530) is a pangenotypic NS5A inhibitor. Collectively, they are in the second generation of HCV therapies.

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.

Glecaprevir was identified by AbbVie and Enanta.

3. Pawlotsky, Gastroenterology 2016
Glecaprevir demonstrates potent pangenotypic activity against HCV *in vitro*

<table>
<thead>
<tr>
<th>Protease Inhibitor</th>
<th>Stable HCV Replicon EC&lt;sub&gt;50&lt;/sub&gt; (nM)</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT2a</th>
<th>GT2b</th>
<th>GT3a</th>
<th>GT4a</th>
<th>GT5a</th>
<th>GT6a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glecaprevir</td>
<td></td>
<td>0.85</td>
<td>0.94</td>
<td>2.2</td>
<td>4.6</td>
<td>1.6</td>
<td>2.8</td>
<td>(0.12)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.86</td>
</tr>
<tr>
<td>Paritaprevir</td>
<td></td>
<td>1.0</td>
<td>0.21</td>
<td>9.8</td>
<td>107</td>
<td>19</td>
<td>0.09</td>
<td>(0.42)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.68</td>
</tr>
<tr>
<td>Simeprevir&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
<td>13</td>
<td>9.4</td>
<td>15</td>
<td>NA</td>
<td>472</td>
<td>NA</td>
<td>36</td>
<td>NA</td>
</tr>
<tr>
<td>Asunaprevir&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
<td>4.0</td>
<td>1.2</td>
<td>230</td>
<td>NA</td>
<td>1162</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Grazoprevir&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td>0.38</td>
<td>0.87</td>
<td>1.3</td>
<td>NA</td>
<td>36</td>
<td>1.2</td>
<td>0.9</td>
<td>0.89</td>
</tr>
<tr>
<td>Voxilaprevir&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
<td>3.9</td>
<td>3.3</td>
<td>3.7</td>
<td>6.6</td>
<td>6.1</td>
<td>2.9</td>
<td>1.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

<sup>a</sup> EC<sub>50</sub> for stable GT5a replicon not available for NS3 protease inhibitors; listed value is EC<sub>50</sub> for transient GT5a replicon.

NA, not available.

1. Simeprevir prescribing information
GLE is potent against common GT1 NS3 substitutions at positions 80, 155, and 168.

A156T/V in GT1 confer resistance to GLE, but these substitutions have low viral fitness and are rarely detected clinically.
## Pibrentasvir

Pibrentasvir demonstrates potent pangenotypic activity against HCV *in vitro*

<table>
<thead>
<tr>
<th>NS5A Inhibitor</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT2a</th>
<th>GT2b</th>
<th>GT3a</th>
<th>GT4a</th>
<th>GT5a</th>
<th>GT6a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pibrentasvir</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Ombitasvir</td>
<td>14</td>
<td>5</td>
<td>12</td>
<td>4</td>
<td>19</td>
<td>2</td>
<td>3</td>
<td>366</td>
</tr>
<tr>
<td>Daclatasvir¹</td>
<td>22</td>
<td>3</td>
<td>13,000</td>
<td>NA</td>
<td>530</td>
<td>13</td>
<td>5</td>
<td>74</td>
</tr>
<tr>
<td>Ledipasvir²</td>
<td>31</td>
<td>4</td>
<td>21,000</td>
<td>16,000</td>
<td>168,000</td>
<td>390</td>
<td>150</td>
<td>1100</td>
</tr>
<tr>
<td>Velpatasvir³</td>
<td>12</td>
<td>15</td>
<td>9</td>
<td>8</td>
<td>12</td>
<td>9</td>
<td>75</td>
<td>6</td>
</tr>
<tr>
<td>Elbasvir⁴</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3000</td>
<td>20</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>MK-8408⁵</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>ACH-3102⁶</td>
<td>26</td>
<td>5</td>
<td>21</td>
<td>~150</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>IDX719⁷</td>
<td>8</td>
<td>3</td>
<td>24</td>
<td>NA</td>
<td>17</td>
<td>2</td>
<td>37</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA, not available.

5. Asante-Appiah E, AASLD, 2014
Activity of Pibrentasvir Against Common GT1 NS5A Substitutions

- PIB demonstrates an improved resistance profile relative to 1\textsuperscript{st} and 2\textsuperscript{nd} generation NS5A inhibitors
  - Highly active against common GT1 NS5A substitutions at positions 28, 30, 31 or 93 that confer resistance to 1\textsuperscript{st} and 2\textsuperscript{nd} generation NS5A inhibitors
  - Retains activity against GT1 \textbf{Y93} substitutions; many 1\textsuperscript{st} and 2\textsuperscript{nd} generation NS5A inhibitors have significantly lower activity against these substitutions
- The superior resistance profile also occurs in other genotypes
Glecaprevir/Pibrentasvir (Mavyret) in Patients with HCV GT1, 2, 4-6 Infection with or without Compensated Cirrhosis

MAVIRET for 8 Weeks in TN/TE NC Patients: ENDURANCE-1 and SURVEYOR-2

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>GT1</th>
<th>GT2</th>
<th>GT4</th>
<th>GT5</th>
<th>GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>606</td>
<td>351</td>
<td>197</td>
<td>46</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>SVR12 (%)</td>
<td>98</td>
<td>99</td>
<td>98</td>
<td>93</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

All analyses are using the ITT population.

TN, treatment-naïve; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; NC, non-cirrhotic; CC, compensated cirrhotic; ITT, intent-to-treat; BT, breakthrough; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

Glecaprevir/Pibrentasvir (Mavyret) in Patients with HCV GT1, 2, 4-6 Infection with or without Compensated Cirrhosis

**MAVIRET for 8 Weeks in TN/TE NC Patients: ENDURANCE-1 and SURVEYOR-2**

<table>
<thead>
<tr>
<th></th>
<th>GT1</th>
<th>GT2</th>
<th>GT4</th>
<th>GT5</th>
<th>GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall SVR12 (%)</td>
<td>99</td>
<td>99</td>
<td>98</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>n</td>
<td>606</td>
<td>351</td>
<td>193</td>
<td>43</td>
<td>2</td>
</tr>
<tr>
<td>Relapse</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Non-VF*</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**MAVIRET for 12 Weeks in TN/TE CC Patients: EXPEDITION-1**

<table>
<thead>
<tr>
<th></th>
<th>GT1</th>
<th>GT2</th>
<th>GT4</th>
<th>GT5</th>
<th>GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall SVR12 (%)</td>
<td>99</td>
<td>99</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>n</td>
<td>146</td>
<td>90</td>
<td>31</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Relapse</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-VF*</td>
<td>7</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All analyses are using the ITT population.

TN, treatment-naïve; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; NC, non-cirrhotic; CC, compensated cirrhotic; ITT, intent-to-treat; BT, breakthrough; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.


Glecaprevir/Pibrentasvir (Mavyret) in Patients with HCV GT3 Infection with or without Compensated Cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>MAVIRET 8 weeks</th>
<th>MAVIRET 12 weeks</th>
<th>DCV + SOF 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12 (%)</td>
<td>95</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td>n</td>
<td>149</td>
<td>222</td>
<td>111</td>
</tr>
<tr>
<td>N</td>
<td>157</td>
<td>233</td>
<td>115</td>
</tr>
<tr>
<td>BT</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Non-VF*</td>
<td>2</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

All analyses are using the ITT population. TN, treatment-naïve; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; BT, breakthrough; CC, compensated cirrhosis; NC, noncirrhotic; DCV, daclatasvir; ESRD, end-stage renal disease; SOF, sofosbuvir; TE, treatment experienced; TN, treatment naive; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

Glecaprevir/Pibrentasvir (Mavyret) in Patients with HCV GT3 Infection with or without Compensated Cirrhosis

**MAVIRET for 8 or 12 Weeks in TN NC Patients: ENDURANCE-3**

- MAVIRET 8 weeks: 95
- MAVIRET 12 weeks: 95
- DCV + SOF 12 weeks: 97

**MAVIRET for 12 Weeks in TN CC Patients, or 16 Weeks in TE NC/CC Patients: SURVEYOR-2 Part 3**

- TN CC: 98
- TE NC/CC: 96

**All analyses are using the ITT population.**

TN, treatment-naïve; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; BT, breakthrough; CC, compensated cirrhosis; NC, noncirrhotic; DCV, daclatasvir; ESRD, end-stage renal disease; SOF, sofosbuvir; TE, treatment experienced; TN, treatment naive; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

**MAVIRET Summary of Product Characteristics; Accessed August 2017.**
8 and 12 Weeks of Glecaprevir / Pibrentasvir in GT1–6 Patients without Cirrhosis (Integrated Analysis)

Integrated efficacy analysis of 8- or 12-weeks Maviret treatment in non-cirrhotic patients with GT1–6 infection across seven phase 2 or 3 clinical trials

Failure rate was similar between 8 and 12 week Maviret®

<table>
<thead>
<tr>
<th>SVR12 (%)</th>
<th>Overall</th>
<th>GT1</th>
<th>GT2</th>
<th>GT3</th>
<th>GT4</th>
<th>GT5</th>
<th>GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 week G/P</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>100</td>
<td>97</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>12 week G/P</td>
<td>99,6</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

BT, breakthrough; mITT, modified intent-to-treat (excludes non-virologic failures); *TE, treatment-experienced (includes patients with prior SOF use); TN, treatment-naive
Includes patients with prior SOF use (8-week Maviret [n = 7] and 12-week Maviret [n = 9]); † All GT3 patients were treatment-naive.

Safety Glecaprevir / Pibrentasvir vs placebo (ENDURANCE-2, in non cirrhotic GT2 patients)


<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>G/P 12 Weeks N = 202</th>
<th>Placebo N = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE*</td>
<td>131 (65)</td>
<td>58 (58)</td>
</tr>
<tr>
<td>AEs leading to study drug discontinuation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAEs</td>
<td>3 (1)†</td>
<td>1 (1)‡</td>
</tr>
<tr>
<td>AEs occurring in ≥10% total patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>24 (12)</td>
<td>12 (12)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>23 (11)</td>
<td>10 (10)</td>
</tr>
</tbody>
</table>

No SAEs were assessed as being related to DAAs, and none led to discontinuation of G/P

* Includes all AEs regardless of relation to study drugs;
† One patient each experienced a broken ankle, hemorrhoids, and a bile duct stone;
‡ Rheumatoid arthritis; § Patient achieved SVR12.

Safety Glecaprevir / Pibrentasvir vs placebo (ENDURANCE-2, in non cirrhotic GT2 patients)

---

**Adverse events**

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>G/P 12 Weeks N = 202</th>
<th>Placebo N = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE*</td>
<td>131 (65)</td>
<td>58 (58)</td>
</tr>
<tr>
<td>AEs leading to study drug discontinuation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAEs</td>
<td>3 (1)†</td>
<td>1 (1)‡</td>
</tr>
<tr>
<td>AEs occurring in ≥10% total patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>24 (12)</td>
<td>12 (12)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>23 (11)</td>
<td>10 (10)</td>
</tr>
</tbody>
</table>

**Laboratory abnormalities**

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>G/P 12 Weeks N = 202</th>
<th>Placebo N = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 (&gt;3 × ULN)</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Grade ≥3 (&gt;5 × ULN)</td>
<td>2 (1)§</td>
<td>1 (1)</td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 (&gt;3 × ULN)</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Grade ≥3 (&gt;5 × ULN)</td>
<td>1 (0.5)§</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (3-10 × ULN)</td>
<td>1 (0.5)</td>
<td>0</td>
</tr>
</tbody>
</table>

No SAEs were assessed as being related to DAAs, and none led to discontinuation of G/P

* Includes all AEs regardless of relation to study drugs;
† One patient each experienced a broken ankle, hemorrhoids, and a bile duct stone;
‡ Rheumatoid arthritis; § Patient achieved SVR12.

### SODAPI study: Response-Guided Therapy

**GT-1b Non-cirrhotic Chinese N=26**

<table>
<thead>
<tr>
<th>Day</th>
<th>0</th>
<th>2</th>
<th>21</th>
<th>35</th>
<th>105</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1:</strong> SOF+LDV+ASV N=12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group 2:</strong> SOF+DCV+SMV N=6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group 3:</strong> SOF+DCV+ASV N=8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Plasma HCV RNA < 500 IU/ml by Day 2

Follow up

*Lau G et al. Lancet Gastro & Hepato 2017*
Pan-Genotypic Diret-Acting Antivirals: Opportunity to Achieve HCV Elimination

1. Introduction
2. Sofosbuvir/Velpatasvir (Epclusa®)
3. Glecaprevir/Pibrentasvir (Mavyret®)
4. HCV Elimination
5. Conclusion
<table>
<thead>
<tr>
<th>Year</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>- F3-F4 (Fibrosis stage) (by any evaluation)</td>
</tr>
<tr>
<td></td>
<td>- Extra-hepatic manifestations</td>
</tr>
<tr>
<td></td>
<td>- HIV/HCV coinfected patients</td>
</tr>
<tr>
<td>2015</td>
<td>- F2 (Fibrosis stage) («severe» F2)</td>
</tr>
<tr>
<td>June 2016</td>
<td>- Transplants</td>
</tr>
<tr>
<td></td>
<td>- Genotype 3</td>
</tr>
<tr>
<td></td>
<td>- At risk of contamination</td>
</tr>
</tbody>
</table>

- **January 2017**: Universal Treatment

---

**Individual Impact**

- (collective Impact)

**Collective Impact**

- (& individual)
Treatment of HCV infections in France

(≈ 20,000 in 2017)

Nb of Patients Treated per months (based on 12 weeks duration per patients)
Oct 2017 (Base GERS)
Majority of Patients with Advanced Fibrosis have been treated (Hepather)
HCC reduction (already a reality)

Nahon P et al. Gastroenterology 2017
Conclusion

• Burden of HCV: Major Public Health Problem
• Global elimination of HCV is now achievable
• HCV cure has a positive impact by:
  – Improving survival
  – Decreasing the incidence of cirrhosis
  – Decreasing hepatocellular carcinoma
  – Improving overall quality of life for patients with HCV
• Multiple common barriers exist for implementation of programs to control HCV across low, middle, and high income countries
• We must continue to be active in our respective countries with increasing screening and linkage to care for all patients
The need to take care of all Humans, No patient left behind

Asselah et al. Eliminating Hepatitis C within Low Income Countries – the need to cure Genotypes 4, 5, 6. Journal of Hepatology, 2018 in press

Hutin J-F, Suisse, WHO, EASL 2017

Incidence rate (per 100,000)

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Map key</th>
<th>Best estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>[Red]</td>
<td>31,0</td>
</tr>
<tr>
<td>America</td>
<td>[Blue]</td>
<td>6,4</td>
</tr>
<tr>
<td>Middle East</td>
<td>[Green]</td>
<td>62,5</td>
</tr>
<tr>
<td>Europa</td>
<td>[Green]</td>
<td>61,8</td>
</tr>
<tr>
<td>South East Asia</td>
<td>[Green]</td>
<td>14,8</td>
</tr>
<tr>
<td>West Pacific</td>
<td>[Blue]</td>
<td>6,0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>23,7</td>
</tr>
</tbody>
</table>

Asselah et al. Eliminating Hepatitis C within Low Income Countries – the need to cure Genotypes 4, 5, 6. Journal of Hepatology, 2018 in press