Grazoprevir (GZR; MK-5172) + Elbasvir (EBR; MK-8742)

Future Treatment Option
New Fixed Dose Combination: GZR/EBR

- **Grazoprevir** (MK-5172)
  - HCV NS3/4A inhibitor
  - 100 mg once daily, oral

- **Elbasvir** (MK-8742)
  - HCV NS5A inhibitor
  - 50 mg once daily, oral

- Broad *in vitro* activity against most HCV genotypes\(^1-3\)
- Retains *in vitro* activity against many clinically relevant RAVs\(^1-3\)

Abstract G07

The Phase 3 C-EDGE Treatment-Naïve Study of a 12-Week Oral Regimen of Grazoprevir (GZR; MK-5172)/Elbasvir (EBR; MK-8742) in Patients With Chronic HCV GT 1, 4 or 6 Infection

S. Zeuzem et al
SVR 12: Full Analysis Set

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>GT 1a</th>
<th>GT 1b</th>
<th>GT 4</th>
<th>GT 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>299/316</td>
<td>144/157</td>
<td>129/131</td>
<td>18/18</td>
<td>8/10</td>
</tr>
<tr>
<td>Non-virologic failure</td>
<td>95%</td>
<td>92%</td>
<td>99%</td>
<td>100%</td>
<td>80%</td>
</tr>
<tr>
<td>Breakthrough</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Relapse</td>
<td>12</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Zeuzem et al., Abstract #G07, EASL 2015
Abstract O001

C-SALVAGE: Grazoprevir (GZR; MK-5172), Elbasvir (EBR; MK-8742) and Ribavirin (RBV) for Chronic HCV-Genotype 1 Infection After Failure of Direct Acting Antiviral (DAA) Therapy

X. Forns et al
### GZR + EBR + RBV x 12 Weeks: SVR12 By Subgroup

<table>
<thead>
<tr>
<th>All Subjects</th>
<th>N = 79</th>
<th>SVR12</th>
<th>76 (96.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse</td>
<td>3 (3.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By Prior PI Therapy</td>
<td></td>
<td>Boceprevir</td>
<td>27/28 (96%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Telaprevir</td>
<td>41/43 (95%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simeprevir</td>
<td>8/8 (100%)</td>
</tr>
<tr>
<td>By Prior Failure Category</td>
<td></td>
<td>On treatment failure</td>
<td>38/40 (95%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapse</td>
<td>25/26 (96%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intolerance</td>
<td>13/13 (100%)</td>
</tr>
<tr>
<td>By Time Since Therapy</td>
<td></td>
<td>&lt;1.1 year</td>
<td>22/24 (92%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥1.1 year</td>
<td>46/46 (100%)</td>
</tr>
<tr>
<td>By Presence of NS3 RAVs</td>
<td></td>
<td>Absent</td>
<td>43/43 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Present</td>
<td>31/34 (91%)</td>
</tr>
</tbody>
</table>

#### By Genotype
- **G1a**: 28/30 (93%)
- **G1b**: 48/49 (98%)

#### By Cirrhosis
- **Yes**: 32/34 (94%)
- **No**: 44/45 (98%)

#### By Viral Load
- ≤800,000 IU/mL: 27/29 (93%)
- >800,000 IU/mL: 49/50 (98%)

- Highly efficacious in patients who failed first generation protease inhibitor/PEG/RBV treatment
Advanced Chronic Kidney Disease
Review of New Data
Abstract L-01

Safety of Ombitasvir/Paritaprevir/Ritonavir Plus Dasabuvir for Treating HCV GT 1 Infection in Patients With Severe Renal Impairment or End-Stage Renal Disease: The RUBY-1 Study

P. Pockros et al
Background/Objectives

- 12 weeks of OBV/PTV/r + DSV
  - GT 1 treatment-naïve
    - Included RBV for GT 1a
    - No RBV for GT 1b
  - CKD stage 4/5, including 60% on hemodialysis
  - Excluded cirrhotics
Summary

• Regimen has been well tolerated, including those on hemodialysis, with or without RBV
• Hemoglobin reductions were managed with monitoring and RBV dose interruption (8/13) and erythropoietin use (4/13)
• No virologic failures to date and all 10 subjects who reached PTW4
Abstract LP-02

C-SURFER: Grazoprevir Plus Elbasvir in Treatment-naïve and Treatment-experienced Patients With HCV GT 1 Infection and Chronic Kidney Disease

D. Roth et al
Background/Objectives

• <1% of GZR and EBR is renally excreted
• This study evaluated GZR+EBR in HCV-infected patients with CrCl<30 mL/min, including patients on hemodialysis
  – GT 1 treatment-naïve or treatment-experienced
  – CKD stage 4/5
  – Included compensated cirrhotics
SVR12: GZR/EBR for 12 Weeks in GT1 Patients With Chronic Kidney Disease

![Graph showing SVR12 results for Modified Full Analysis Set 16 Weeks and Full Analysis Set 24 Weeks.](Image)

<table>
<thead>
<tr>
<th>Relapse</th>
<th>Modified Full Analysis Set 16 Weeks</th>
<th>Full Analysis Set 24 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Discontinued unrelated to treatment</td>
<td>0</td>
<td>6&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Noncirrhotic, interferon-intolerant patient with HCV GT1b infection relapsed at FW12.

<sup>b</sup>Lost to follow-up (n = 2), n = 1 each for death, noncompliance, withdrawal by subject, and withdrawal by physician (owing to violent behavior).

- GZR/EBR was generally safe and well tolerated.
How Do We Currently Manage HCV-infected Patients With CKD Stage 4/5?

Are We Concerned With Using RBV For GT 1a Patients?
GT 3 Update
Abstract L-05

Sofosbuvir Plus Peg-IFN/RBV for 12 Weeks vs Sofosbuvir/RBV for 16 or 24 Weeks in Genotype 3 HCV-Infected Patients and Treatment-experienced Cirrhotic Patients With Genotype 2 HCV: The BOSON Study

G. Foster et al
Study Design

- Multicenter study, open-label, randomized (1:1:1) study at 80 sites in UK, Australia, USA, Canada, and New Zealand
- GT 2 patients: treatment experienced (TE) with cirrhosis
- GT 3 patients: TE or treatment naïve (TN), with or without cirrhosis
- Stratification
  - Cirrhosis
  - HCV Genotype
  - Prior HCV treatment
- Platelets ≥60,000 cells/mm³

Foster et al., Abstract #L-05, EASL 2015
Overall SVR12 (GT 2 and GT 3 Combined)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weeks</th>
<th>SVR12 (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>16</td>
<td>72/196</td>
<td>0.0013</td>
</tr>
<tr>
<td>SOF + RBV</td>
<td>24</td>
<td>85/199</td>
<td>0.023</td>
</tr>
<tr>
<td>SOF + PEG/RBV</td>
<td>12</td>
<td>93/197</td>
<td></td>
</tr>
</tbody>
</table>

Error bars represent 95% confidence intervals.
Foster et al., Abstract #L-05, EASL 2015
SVR12: GT 2 vs GT 3

Error bars represent 95% confidence intervals.

Foster et al., Abstract #L-05, EASL 2015
SVR12 in GT 3 by Treatment History and Cirrhosis Status

<table>
<thead>
<tr>
<th>Treatment History</th>
<th>Cirrhosis Status</th>
<th>SOF + RBV 16 weeks</th>
<th>SOF + RBV 24 weeks</th>
<th>SOF + PEG/RBV 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Naïve</td>
<td>No Cirrhosis</td>
<td>58/70</td>
<td>65/72</td>
<td>68/71</td>
</tr>
<tr>
<td></td>
<td>Cirrhosis</td>
<td>12/21</td>
<td>18/22</td>
<td>21/23</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced</td>
<td>41/54</td>
<td>44/54</td>
<td>49/52</td>
</tr>
<tr>
<td></td>
<td>No Cirrhosis</td>
<td>17/36</td>
<td>26/34</td>
<td>30/35</td>
</tr>
<tr>
<td></td>
<td>Cirrhosis</td>
<td>47</td>
<td>77</td>
<td>86</td>
</tr>
</tbody>
</table>

Foster et al., Abstract #L-05, EASL 2015
Abstract LP-05

Daclatasvir Plus Sofosbuvir With or Without Ribavirin in Patients With HCV Genotype 3 Infection: Interim Analysis of a French Multicenter Compassionate Use Program

C. Hezode et al
SVR4: DCV/SOF ± RBV in GT 3 Patients (12 vs 24 Weeks)

EASL Recommendation: GT 3 cirrhotics should receive SOF/DCV + RBV for 24 weeks

Hezode et al., Abstract #LP-05, EASL 2015
Is SOF + PEG/RBV for 12 Weeks Standard of Care for GT 3?
Can We Shorten Treatment Duration of SMV/SOF?
SVR12: SMV/SOF in GT 1 Non-cirrhotics (8 vs 12 Weeks)

Proportion of patients (%)

Treatment-naïve

SMV+SOF 12 weeks

97

112/115

SMV+SOF 8 weeks

85

88/103

Treatment-experienced

SMV+SOF 12 weeks

95

38/40

SMV+SOF 8 weeks

77

40/52

GT1a

97

112/116

79

92/116

73

44/46

36/49

GT1a with Q80k

97

68/70

84

56/67

GT1a without Q80k

97

38/39

92

36/39

GT1b

Kwo et al., Abstract #LP-14, EASL 2015
Can We Shorten Treatment Durations to <12 Weeks By Combining Potent DAAs from Different Classes?
Abstract O006

C-SWIFT: Grazoprevir/Elbasvir + Sofosbuvir in Cirrhotic and Noncirrhotic Treatment-naive Patients With Hepatitis C Virus GT 1 Infection, for Durations of 4, 6 or 8 Weeks and GT 3 Infection for Durations of 8 or 12 Weeks

F. Poordad et al
SVR12 in GT 1 Treatment-naïve Patients

**Non-cirrhotic**
- 4 weeks: 33%
- 6 weeks: 87%
- 8 weeks: 94%

**Cirrhotic**
- 4 weeks: 10/30*
- 6 weeks: 26/30
- 8 weeks: 16/20

**Breakthrough**
- 4 weeks: 0
- 6 weeks: 0
- 6 weeks: 0
- 8 weeks: 0

**Relapse**
- 4 weeks: 20
- 6 weeks: 4
- 6 weeks: 4
- 8 weeks: 1

**Excluded**
- 4 weeks: 1
- 6 weeks: 0
- 6 weeks: 0
- 8 weeks: 3†

*Excluded patients who discontinued due to reasons other than virologic failure
† One of the 3 patients who discontinued had HCV G2 at discontinuation

Poordad et al., Abstract #O006, EASL 2015
SVR12 in GT 3 Treatment-naïve Patients

mITT analysis excluded patients who discontinued early due to reasons other than virologic failure

Poordad et al., Abstract #O006, EASL 2015
Safety and Efficacy of Short-Duration Treatment With GS-9857 Combined With Sofosbuvir/GS-5816 in Treatment-Naïve and DAA-Experienced Genotype 1 Patients With and Without Cirrhosis

E. Gane et al
SOF/GS-5816 (2nd Gen NS5A Inhibitor) + GS-9857 (Protease Inhibitor): SVR12 in GT 1 Patients

All failures were due to relapse

Treatment Naïve No Cirrhosis

- 4 weeks: 27% (4/15)
- 6 weeks: 93% (14/15)

Treatment Naïve Cirrhosis

- 6 weeks: 87% (13/15)

Prior DAA Failure + Cirrhosis

- 6 weeks: 67% (20/30)

SOF/GS-5816 FDC + GS-9857

Gane et al., Abstract #LP-05, EASL 2015
Are There Long-Term Consequences of Treating for Too Short?
Abstract O005

Retreatment of Patients Who Failed 8 or 12 Weeks of Ledipasvir/Sofosbuvir-Based Regimens With Ledipasvir/Sofosbuvir for 24 Weeks

E. Lawitz et al
SVR12 by Subgroup

- Overall SVR12 = 71% (29/41)

<table>
<thead>
<tr>
<th>Cirrhosis</th>
<th>No</th>
<th>Yes</th>
<th>Prior Treatment Duration</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15/22</td>
<td>14/19</td>
<td>8 wks</td>
<td>24/30</td>
<td>5/11</td>
</tr>
<tr>
<td></td>
<td>11/11</td>
<td>18/30</td>
<td>12 wks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All 11 patients without NS5A RAVs received 8 weeks of prior treatment

Lawitz et al., Abstract #O005, EASL 2015
How Do We Best Manage Patients with NS5A RAVs?

Should All Patients Have Baseline RAV Testing?

How Long Before Retreating a Patient with RAVs?
Advanced Cirrhosis/Post-OLT
Regimens With New Data

- **SOLAR 2: SOF/LDV/RBV (G02; Manns, et al)**
  - 12 vs 24 week treatment
  - GT 1 and GT 4 CPT B&C
  - SVR12: 88% (57/65) (12 wk arm) vs 89% (54/61) (24 wk arm)
SVR 12: GT 1 Pre- and Post-Transplant CPT B and C

LDV/SOF + RBV  
- **12 Weeks**
- **24 Weeks**

### GT 1 Pre-Transplant

- **CPT B**
  - 87% (20/23)
  - 96% (22/23)
- **CPT C**
  - 85% (17/20)
  - 72% (13/18)

### GT 1 Post-Transplant

- **CPT B**
  - 95% (19/20)
  - 100% (16/16)
- **CPT C**
  - 50% (1/2)
  - 75% (3/4)

27 subjects in the 24 week arm have not reached SVR12; 7 subjects who were transplanted and 3 subjects did not meet inclusion criteria are excluded. Error bars represent 2-sided exact 90% confidence intervals.

Manns et al., Abstract #G02, EASL 2015
Regimens With New Data

• UK EAP: SOF + LDV or DCV ± RBV (O002; Foster, et al)
  – 12 week treatment
  – GT 1 and GT 3 CP-B and C patients (Mean MELD=11.9)
  – Virologically effective with >40% showing improvement in liver function
  – For patients <65 years if albumin is >35 g/L, improvement in liver function is more likely than harm
Regimens With New Data

• ALLY 1: DCV/SOF/RBV (L-08; Poordad, et al)
  – 12 week treatment
  – Any genotype enrolled but predominantly GT 1
  – Advanced cirrhosis (CPT A, B and C patients) and post-OLT
  – SVR12: CPT A=92% (11/12), CPT B=94% (30/32), CPT C=56% (9/16) and post-OLT=94% (50/53)

• C-SALT: GZR/EBR (O008; Jacobson, et al)
  – 12 week treatment
  – GT 1 CPT B patients (Mean MELD=9.9)
  – SVR12: 90% (27/30)
Advantages vs Disadvantages of Treating Advanced Cirrhosis vs Post-OLT
“EASL Recommendations on Treatment of Hepatitis C 2015” issued this week (J Hep). Is there any impact on current practice?
This activity is supported by educational grants from AbbVie, Bristol-Myers Squibb, and Gilead Sciences.