A Phase 3, French Multicenter, Open-Label Study to Investigate the Efficacy of Elbasvir/Grazoprevir Fixed-Dose Combination for 8 Weeks in Treatment-Naïve HCV GT1b-Infected Patients, with non-severe fibrosis: the STREAGER study

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Disclosures

• Abbvie: travel expenses and honoraria for teaching and board membership
• BMS: honoraria for teaching
• Gilead: travel expenses and honoraria for teaching and board membership
• MSD: travel expenses and honoraria for teaching and board membership

• The study was sponsored by MSD
Introduction

- Genotype 1b is the most common subtype of HCV infection, responsible for 22% of all infections world-wide

Gower et al. *J Hepatol.* 2014;61:S45-S57
Adult viraemic patients infected by GT1b around the world

North America 730,000
North Africa/Middle East 990,000
Latin America 1,900,000
Europe 4,250,000
China 8,600,000
South Africa 140,000
Japan 814,000
Australia 40,000

Gower et al. J Hepatol. 2014;61:S45-S57
Adult viraemic patients infected by GT1b in Europe

Western Europe: 800,000
Central Europe: 640,000
Eastern Europe: 3,100,000

Gower et al. J Hepatol. 2014;61:S45-S57
Elbasvir and Grazoprevir

- HCV NS5A inhibitor, 50 mg
- HCV NS3/4A inhibitor, 100 mg

A once-daily, fixed-dose combination tablet for the treatment of patients with HCV GT1 or 4 infection

- Broad activity versus most HCV genotypes \textit{in vitro}\textsuperscript{2-4}
- Efficacious in treatment-naive & treatment-experienced patients, cirrhotic and non-cirrhotic patients, HIV/HCV co-infected patients and chronic kidney disease\textsuperscript{5-7}

- Approved in Europe, US, Canada, and other countries worldwide

\textsuperscript{1. Zepatier [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; 2016.}
\textsuperscript{7. Roth D et al. Lancet. 2015;38:1537-1545.}
Grazoprevir/Elbasvir: SVR12
Genotype 1b in experienced (TE) and cirrhosis

### TN vs TE

- **TN:**
  - EBR/GZR 12 weeks: 97%
  - Number of patients: 828/851

- **TE:**
  - EBR/GZR 12 weeks: 97%
  - Number of patients: 212/219

### No cirrhosis vs cirrhosis

- **No cirrhosis:**
  - EBR/GZR 12 weeks: 97%
  - Number of patients: 852/881

- **Cirrhosis:**
  - EBR/GZR 12 weeks: 99.5%
  - Number of patients: 188/189

Zeuzeum AASLD 2016, abs 874
Grazoprevir/Elbasvir +/- RBV: SVR12
genotype 1b naïve patients treated 8 weeks (C Worthy)

<table>
<thead>
<tr>
<th>Stage</th>
<th>SVR12 ITT</th>
<th>Relapse</th>
<th>Lost to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0-F3</td>
<td>92% (56/61)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>F0-F2</td>
<td>96% (54/56)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>F3</td>
<td>40% (2/5)</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
Grazoprevir/Elbasvir +/- RBV: SVR12
genotype 1b naïve patients treated 8 weeks (C Worthy)

SVR12 mITT

- F0-F3: 93% (56/60)
- F0-F2: 98% (54/55)
- F3: 40% (2/5)
Aim

Evaluate the efficacy and safety of Elbasvir/Grazoprevir Fixed-Dose Combination for 8 Weeks in Treatment-Naïve, HCV GT1b-Infected Patients, with non-severe fibrosis
Methods

• Inclusion criteria

  • Patients were treatment-naïve, GT1b, without HIV/HBV co-infection

  • Non severe fibrosis ($F \leq 2$) was diagnosed according to a combination of two tests (*J Boursier database, Angers*):

    • Fibroscan® lower than 9.5 kPa AND Fibrotest® lower than 0.59
Study design

N = 120

Day 1 | Week 8 | Week 32
---|---|---
ELB/GZR | SVR 4 | SVR 24

How to use the package:
- Take one pill every day.
- This package will last you for 2 weeks (36 days).

Zepatier™
(Elbasvir and grazoprevir) tablets
- 50 mg/100 mg
- 14 tablets
- Take one pill every day
- Push and hold, then pull until tablet comes out.
### Demographics

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=74</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>48 (65)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>54 (12.6)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>24.3 (3.9)</td>
</tr>
<tr>
<td>ALAT &gt; N, n (%)</td>
<td>30 (41)</td>
</tr>
<tr>
<td>Baseline viral load, n (%)</td>
<td></td>
</tr>
<tr>
<td>≤800,000 IU/mL</td>
<td>28 (38)</td>
</tr>
<tr>
<td>&gt;800,000 IU/mL</td>
<td>46 (62)</td>
</tr>
<tr>
<td>Fibrosis:</td>
<td></td>
</tr>
<tr>
<td>Fibroscan® (F0-F1 &lt;7,1kPa), n (%)</td>
<td>65 (88)</td>
</tr>
<tr>
<td>Fibrotest® (F0-F1 &lt;0,32), n (%)</td>
<td>44 (59)</td>
</tr>
<tr>
<td>APRI &lt; 1, n (%)</td>
<td>73 (99)</td>
</tr>
<tr>
<td>FIB-4 &lt; 1.45 , n (%)</td>
<td>46 (62)</td>
</tr>
<tr>
<td>FIB-4 &lt; 2.5 , n (%)</td>
<td>73 (99)</td>
</tr>
</tbody>
</table>
**Results (1)**

<table>
<thead>
<tr>
<th></th>
<th>SVR4</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Lost-to-follow up (LTFU)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

97% 72/74

96% 71/74
## Results (2)

### Characteristics of the 3 relapsers

<table>
<thead>
<tr>
<th>Patient</th>
<th>BMI Kg/m²</th>
<th>ALT ULN</th>
<th>Viral load IU/mL</th>
<th>Fibrosis Score</th>
<th>Genotype at relapse</th>
<th>RAS at relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>27.2</td>
<td>1.8</td>
<td>453.899</td>
<td>9.1 kPa (F2)</td>
<td>1e</td>
<td>L28M, R30Q, A92T, Y93H</td>
</tr>
<tr>
<td>Patient 2</td>
<td>31.4</td>
<td>1.6</td>
<td><strong>14.000.000</strong></td>
<td>6.4 kPa (F0-F1)</td>
<td>1b</td>
<td>Y93H</td>
</tr>
<tr>
<td>Patient 3</td>
<td>25.5</td>
<td>0.7</td>
<td><strong>16.437.573</strong></td>
<td>5.1 kPa (F0-F1)</td>
<td>1b</td>
<td>L31M, Y93H</td>
</tr>
</tbody>
</table>
Results (3)

After exclusion of the patient with genotype 1e

<table>
<thead>
<tr>
<th></th>
<th>SVR4</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>LTFU</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

SVR4: 99% 72/73
SVR12: 97% 71/73
Safety

- An 8-week regimen of EBR/GZR was well-tolerated with a favorable safety profile

- No adverse event grade 3 or 4 was observed

- The main adverse events with a frequency higher than 10% were:
  - asthenia (26%)
  - headache (23%)
  - digestive disorders (14%)
Conclusions

- High cure rate (SVR12=97%) was achieved in a treatment-naïve non severe fibrosis GT1b-infected population treated by the combination of grazoprevir and elbasvir for 8 weeks.

- Our results are in agreement with the results obtained in the C-Worthy study (SVR12=98%) in patients treated for 8 weeks.

- These results are very similar to those obtained in patients treated for 12 weeks (SVR12=97%).

- These results are preliminary. Final study results on 120 patients to come next spring 2018.
Thanks to:
-the patients
-all the investigators from the 14 centers

- Angers Isabelle Fouchart-Hubert
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- Lille Valérie Canva
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- Lyon François Bailly
- Montpellier Dominique Larrey
- Nantes Jérôme Gournay
- Nice Albert Tran
- Paul Brousse Didier Samuel
- Toulouse Sophie Métivier
Kona in December

Clermont Ferrand in December