High Efficiency in Patients With Chronic Hepatitis C Virus (HCV) Genotype 1b Infection Treated with Elbasvir/Grazoprevir for 12 Weeks: An Integrated Analysis

**Background**
- Genotype G1b/G1 is the most common subtype of hepatitis C virus (HCV) infection, responsible for 22% of all infections worldwide.
- Significant regional variability:
  - 20% of cases in North America
  - 30% of cases in Latin America
  - 50% of cases in Europe
  - Common in many countries throughout Asia
  - 40% of infections in Taiwan and South Korea

- Elbasvir (GZR) is a once-daily NS5A inhibitor and grazoprevir (GZO) is a once-daily NS3/4A protease inhibitor.
- Approved in Europe, the United States, Canada, and other countries worldwide.
- Broad activity vs most HCV genotypes in vitro.

**Patients and Methods**

**Study Design**
- Retrospective integrated post hoc analysis of data from 11 clinical trials in the GZO/GZR phase 2/3 clinical development program, enrolling 3020 treatment-naive patients worldwide.
- Patients were treatment-naive or treatment-experienced, and included those with compensated cirrhosis or HIV coinfection.
- Patients with decompensated liver disease or evidence of hepatocellular carcinoma were excluded.
- The primary endpoint of all 11 studies was SVR12.
- In phase 3 studies, patients were treated with a fixed-dose combination of GZ/GZ, and in phase 2 studies, patients were individually dosed.
- Full analysis set (FAS) includes all patients who received at least one dose of study medication.
- Modified FAS (mFAS) excludes patients with nonsustained virologic failure.
- Population sequencing was performed at baseline and at the time of virologic failure.
- The specific NS5A loci evaluated were any polymorphism at amino acid positions 28, 30, and 31.

**Methods**
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**Results**

**Virologic Response**
- In the FAS population, 97.2% (1010/1040) of patients with HCV GT1b infection receiving EBR/GZR for 12 weeks achieved SVR12 (Figure 5) (SVR12 in the mFAS population was 99.6% (1040/1055).

**Table 1. Patient demographics**

<table>
<thead>
<tr>
<th>Race</th>
<th>All patients</th>
<th>FAS (N = 1070)</th>
<th>mFAS (N = 1070)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>462 (43.2)</td>
<td>496 (47.6)</td>
<td>519 (48.6)</td>
</tr>
<tr>
<td>African-American</td>
<td>95 (9.0)</td>
<td>106 (9.8)</td>
<td>110 (10.3)</td>
</tr>
<tr>
<td>White</td>
<td>482 (45.4)</td>
<td>526 (48.9)</td>
<td>540 (50.2)</td>
</tr>
<tr>
<td>Other/missing</td>
<td>9 (0.8)</td>
<td>11 (0.8)</td>
<td>17 (1.6)</td>
</tr>
<tr>
<td>Male</td>
<td>570 (53.4)</td>
<td>596 (56.3)</td>
<td>613 (57.1)</td>
</tr>
<tr>
<td>Female</td>
<td>492 (46.0)</td>
<td>475 (43.7)</td>
<td>457 (42.9)</td>
</tr>
</tbody>
</table>

**Table 2. Baseline metabolic profile of patients with HCV infection**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FAS (N = 1070)</th>
<th>mFAS (N = 1070)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>25.1 (5.6)</td>
<td>25.1 (5.6)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>186 (56.0)</td>
<td>186 (56.0)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>114 (61.8)</td>
<td>114 (61.8)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>45 (42.1)</td>
<td>44 (41.6)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>103 (95.2)</td>
<td>103 (95.2)</td>
</tr>
</tbody>
</table>

**Figure 4. SVR12 subgroup analyses shown in Figure 4**

**Figure 5. Prevalence and impact on SVR12 of baseline NS5A RAVs at position Y93**

**Conclusions**
- This integrated analysis of 1070 patients demonstrated EBR/GZR for 12 weeks was highly efficacious in patients with HCV GT1b infection.
- The overall SVR12 was 97.2% (FAS population).
- SVR12 was 96.6% in the mFAS population, which excluded patients with nonsustained virologic failure.
- SVR12 rates were high regardless of race, age, treatment-experienced or baseline, and presence of cirrhosis, HIV coinfection, or presence of baseline NS5A RAVs.
- EBR/GZR demonstrated a favorable safety profile.
- The rates of SAEs were comparable between those treated with EBR/GZR or placebo.
- All-cause AEs were detected in 11% of patients, comparable to the rate in the overall population of all patients treated with EBR/GZR for 12 weeks.
- Further investigation of shorter durations regimens for GT1b patients with advanced cirrhosis.

**References**


**Figure 2. Geographic distribution of enrolled patients**

**Figure 3. SVR12**

**Figure 4. SVR12 subgroup analyses shown in Figure 4**

**Figure 5. Prevalence and impact on SVR12 of baseline NS5A RAVs at position Y93**

**Figure 6. SVR12**

**Acknowledgments**
- We extend our gratitude to the patients, their families, investigators, and site personal who participated in this study.
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