DAA Failures
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MAGELLAN-1, Part 2:
Glecaprevir/Pibrentasvir for 12 or 16 Weeks in Patients with Chronic HCV Genotype 1 or 4 and Prior Direct-Acting Antiviral Treatment Failure
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Abstract PS-156
Next Generation Direct-Acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A
protease inhibitor

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A
inhibitor

Coformulated: G/P

• Once-daily oral dosing with food
• Potent against common NS3 and NS5A polymorphisms
• Minimal metabolism, primary biliary excretion, and negligible renal excretion (<1%)
  • Favorable safety profile: mostly mild AEs with few Grade ≥3 lab abnormalities
  • Concomitant PPI use allowed
  • Phase 2 (12 weeks): 95% mITT SVR12 rate in patients with prior NS5A and/or PI failure

Glecaprevir (formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Pibrentasvir (formerly ABT-530)
pangenotypic NS5A inhibitor

MAGELLAN-1, Part 2 Study: Objective and Study Design

Objective
• Determine the efficacy and safety of G/P for 12 or 16 weeks in patients with chronic HCV GT1, 4, 5 or 6 infection and prior DAA failure, including those with compensated cirrhosis

Weeks

Treatment Period

12 weeks
N = 44
G/P

16 weeks
N = 47
G/P

Patients with cirrhosis: 50% enrollment maximum
NS5A-naive patients: 40% enrollment maximum

SVR12
### MAGELLAN-1, Part 2 Study: Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>G/P 12 weeks N = 44</th>
<th>G/P 16 weeks N = 47</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>31 (70)</td>
<td>33 (70)</td>
</tr>
<tr>
<td>White race, n (%)</td>
<td>34 (77)</td>
<td>35 (76)</td>
</tr>
<tr>
<td>Black race, n (%)</td>
<td>9 (20)</td>
<td>11 (23)</td>
</tr>
<tr>
<td>Age, median years (range)</td>
<td>57 (22 – 67)</td>
<td>56 (36 – 70)</td>
</tr>
<tr>
<td>BMI, median kg/m² (range)</td>
<td>28 (21 – 41)</td>
<td>29 (20 – 52)</td>
</tr>
<tr>
<td>HCV RNA, median log₁₀ IU/mL (range)</td>
<td>6.1 (4.7 – 7.2)</td>
<td>6.3 (4.7 – 7.1)</td>
</tr>
<tr>
<td>Compensated cirrhosis, n (%)</td>
<td>15 (34)</td>
<td>12 (26)</td>
</tr>
<tr>
<td>HCV subtype*, n (%)</td>
<td>1a 35 (80)</td>
<td>32 (71)</td>
</tr>
<tr>
<td></td>
<td>1b 8 (18)</td>
<td>10 (22)</td>
</tr>
<tr>
<td></td>
<td>1e 0</td>
<td>1 (2)</td>
</tr>
<tr>
<td></td>
<td>4 1 (2)</td>
<td>3 (6)</td>
</tr>
<tr>
<td></td>
<td>1 (not subtyped)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1† (2)</td>
</tr>
</tbody>
</table>

*Genotype and subtype determined by phylogenetic analysis for samples with available sequences.
†One patient had GT1, based on LiPA analysis, but was not subtyped.

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### MAGELLAN-1, Part 2 Study: Clinical Characteristics (Cont’d)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>G/P 12 weeks N = 44</th>
<th>G/P 16 weeks N = 47</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous DAA regimen class*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NS3/4A PI only (NS5A inhibitor-naïve)</td>
<td>14 (32)</td>
<td>13 (28)</td>
</tr>
<tr>
<td>NS5A inhibitor only (PI-naïve)</td>
<td>16 (36)</td>
<td>18 (38)</td>
</tr>
<tr>
<td>NS3/4A PI + NS5A inhibitor</td>
<td>14 (32)</td>
<td>16 (34)</td>
</tr>
<tr>
<td>Prior DAA treatment response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>On-treatment failure</td>
<td>14 (32)</td>
<td>13 (28)</td>
</tr>
<tr>
<td>Virologic relapse</td>
<td>30 (68)</td>
<td>34 (72)</td>
</tr>
<tr>
<td>Presence of key baseline substitutions†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>13 (30)</td>
<td>13 (30)</td>
</tr>
<tr>
<td>NS3 only</td>
<td>2 (5)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>NS5A only</td>
<td>24 (55)</td>
<td>23 (52)</td>
</tr>
<tr>
<td>NS3 + NS5A</td>
<td>5 (11)</td>
<td>4 (9)</td>
</tr>
</tbody>
</table>

NS3 PIs included: PTV, SVR, ASS, TVR, or SOF; NS5A inhibitors included: DCV, LDV, or OBV.
Sofosbuvir (NS5B inhibitor) could be included in any prior treatment regimen.
‡Only 44 patients had sequencing data available in each arm; percentages are based on N = 44; 2 substitutions detected by next generation sequencing using 10% detection threshold at positions 155, 156, and 168 in NS3, and 24, 28, 30, 31, 58, 92, and 93 in NS5A.

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Over all SVR12:
- 12-week: 89% (39/44)
- 1 OTVF; 4 relapse
- 16-week: 91% (43/47)
- 1 OTVF; 0 relapse

Prior Treatment History
- PI: TVR, SMV, BOC
- NS5A: LDV, DCV
- NS5A+PI: OBV and PTV, or other combinations
- OTVF, on-treatment virologic failure

Key baseline NS3 and NS5A substitutions were only present in patients with prior failure to both PI and NS5A inhibitors
- 5/9 of these patients achieved SVR12
- Key NS3 positions:
  - 155, 156, 168
- Key NS5A positions:
  - 24, 28, 30, 31, 58, 92, 93
- OTVF:
  - on-treatment virologic failure
MAGELLAN-1, Part 2 Study: Conclusions

- Patients with prior failure to PI containing regimens (NS5A inhibitor-naïve):
  - 100% SVR12 with 12 or 16 weeks of G/P treatment
- Patients with prior failure to both PI- and NS5A inhibitor-containing regimens had lower SVR12 rates
- Patients with prior failure to NS5A inhibitors (i.e., LDV or DCV); NS3/4A PI-naïve:
  - 94% SVR12 with 16 weeks of G/P treatment with no relapse
  - No impact of baseline NS5A substitutions on SVR12
- G/P for 12 or 16 weeks was well tolerated; Grade 3 lab abnormalities were rare, with no discontinuations due to AEs, and no DAA-related serious AEs

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