ENDURANCE-1: A Phase 3 Evaluation of the Efficacy and Safety of 8- versus 12-week Treatment with Glecaprevir/ Pibrentasvir (formerly ABT-493/ABT-530) in HCV Genotype 1 Infected Patients with or without HIV-1 Co-infection and without Cirrhosis

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Abstract 253

Next Generation Direct-Acting Antivirals

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

In vitro:1,2

• Additive/synergistic antiviral activity
• High barrier to resistance
• Potent against common NS3 polymorphisms (eg., positions 80, 155, and 168) and NS5A polymorphisms (eg., positions 28, 30, 31 and 93)

Clinical PK & metabolism:

• Once-daily oral dosing
• Minimal metabolism and primary biliary excretion
• Negligible renal excretion (<1%)

Glecaprevir was identified by AbbVie and Enanta.

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 253. 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.
ENDURANCE-1: Study Design and Patient Population

- GT1 non-cirrhotics (n=703)
- Treatment naïve or treatment-experienced with IFN or PEG +/- RBV or SOF + RBV +/- PEG (excluded any prior experience with HCV DAA other than SOF)
- HCV monoinfected or HCV/HIV coinfected (ART naïve or on stable ART regimen)

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 253.

GLE/PIB x 8 Weeks or 12 Weeks in GT1 Noncirrhotics

Primary endpoint threshold: 91%

**ITT-PS**: ITT population, excluding HIV co-infected and SOF experienced patients

**ITT-PS-PP**: ITT-PS population excluding patients with premature D/C or virologic failure prior to week 8, and missing data in the SVR12 window

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 253.
Subgroup Analysis: Pooled ITT Population

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>GT1a</th>
<th>F3 Fibrosis</th>
<th>Treatment experienced</th>
<th>HCV RNA ≥6 million IU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>% SVR12</td>
<td>99</td>
<td>100</td>
<td>100</td>
<td>99</td>
</tr>
</tbody>
</table>

Summary of Laboratory Abnormalities

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>G/P 8 Weeks N = 352</th>
<th>G/P 12 Weeks N = 351</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AST</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 (&gt;3 × ULN)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade ≥3 (&gt;5 × ULN)</td>
<td>1 (0.3)</td>
<td>0</td>
</tr>
<tr>
<td><strong>ALT</strong>*</td>
<td></td>
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</tr>
<tr>
<td>Grade ≥3 (&gt;5 × ULN)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total Bilirubin Grade 3 (3-5 × ULN)</strong>†</td>
<td>1 (0.3)</td>
<td>2 (0.6)</td>
</tr>
</tbody>
</table>

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal
*Post-nadir
†Grade 3 bilirubin elevations observed at baseline, all primarily indirect
No Grade 4 laboratory abnormalities were observed
Safety was similar in HCV GT1 mono-infected and HIV-1/HCV GT1 co-infected patients
All co-infected patients maintained HIV-1 RNA suppression during the treatment period
ENDURANCE-2 Study Design

- In Phase 2 trials, 98% (53/54) SVR12 in GT2-infected patients treated for 8 weeks (no virologic failures); favorable safety with no ALT elevations or dose-dependent AEs
- ENDURANCE-2 (NCT02640482) is a randomized, double-blind, placebo-controlled, multicenter, phase 3 study investigating the safety and efficacy of 12-week G/P in treatment-naïve or treatment-experienced patients with chronic HCV GT2 infection without cirrhosis

ENDURANCE-2: Efficacy, ITT & mITT Populations

**ITT population:** excludes 6 SOF-experienced patients, all of whom achieved SVR12

**mITT population:** ITT population excluding 1 non-virologic failure who achieved SVR4
ENDURANCE-4: Study Design

Open-label, multicenter, single-arm study to evaluate the efficacy and safety of 12-week G/P in HCV FT4, 5, or 6-infected, non-cirrhotic patients

- Key Study Endpoints
  - SVR12
  - Percentage of participants with on-treatment virologic failure or post-treatment relapse
  - Adverse events (AEs) and lab abnormalities

EDURANCE-4 Study: Efficacy Results

G/P is unapproved. The efficacy and safety of the regimen has not been established.

*One GT4 patient discontinued treatment on day 12 and did not achieve SVR12

Asselah T, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 114.
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