Telaprevir Treatment of HIV/HCV Genotype 1 Patients with Severe Fibrosis: Efficacy Results to Week 16

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Background and Aims

- Telaprevir in hepatitis C virus (HCV) treatment-naive patients was approved for the treatment of chronic HCV genotype 1 infection in combination with peginterferon (PI) and ribavirin (RBV).
- HEP-005 is an ongoing, open-label, international clinical trial of telaprevir for patients with hepatocellular carcinoma or cirrhosis (HCC) genotype 1 infection and either severe fibrosis or compensated cirrhosis.
- This interim analysis investigates the safety and efficacy of telaprevir in patients with severe fibrosis in interim Week 18.
- HEP-005 Interim Analysis
  - Design: multi-center, open-label, early-access program of telaprevir in combination with PI.
  - Inclusion: genotype 1 (F3 or F4) compensated cirrhosis (F4), HCV/HCV co-infection.
  - Recruitment: 114 patients were randomized to the telaprevir plus PI for 12 weeks, followed by PI for 36 weeks. Data to Week 16 available for 102 patients were included in the interim analysis.

Methods

- To be eligible, patients must have been in the early access program, each patient must have satisfied the following criteria:
  - Male or female, between the ages of 18 and 70
  - HCV genotype 1b with a quantifiable plasma HCV RNA
  - On PI-IFN/RBV treatment for more than 8 weeks before Day 1 without switches
  - Baseline HIV viral load <800,000 IU/mL
  - Baseline HIV RNA at baseline
  - Have compensated liver disease (Child-Pugh Grade A)
  - Have HCV genotype 1 with a quantifiable plasma HCV RNA
  - Rapid virologic response (rVR) was defined as HCV RNA <50 copies/mL at Week 8.
  - Baseline fibrosis stage ≥F2 (bridging fibrosis, F2).
  - HBV co-infection.
  - RBV dose ≥250 mg/day.

Results

- Of the 102 patients randomized, 85 (84%) had undetectable HCV RNA by Week 12, with 80 (80%) achieving undetectable HCV RNA by Week 24 (Table 1 and Figure 4).
- Eight (8%) patients had detectable HCV RNA at Week 24 (Figure 4).
- Of these 8 patients, 6 (6%) had HCV RNA >50 copies/mL and 2 (2%) had HCV RNA <50 copies/mL.
- The mean viral load at baseline was 1000 (n=6), 8000 (n=2), and 80000 (n=1) copies/mL.
- Six (6%) patients discontinued treatment due to adverse events.
- The most common adverse events were gastrointestinal, 28% had Grade 3 nausea.
- The most common adverse events were headache, 8% had Grade 3 headache.
- Of the 102 patients randomized, 81 (80%) had HCV RNA <25 IU/mL undetectable at Week 12
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Efficacy data

- Of the 102 patients enrolled, 85 (84%) had undetectable HCV RNA by Week 12, with 80 (80%) achieving undetectable HCV RNA by Week 24 (Table 1 and Figure 4).
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Safety data

- The mean viral load at baseline was 1000 (n=6), 8000 (n=2), and 80000 (n=1) copies/mL.
- Six (6%) patients discontinued treatment due to adverse events.
- The most common adverse events were gastrointestinal, 28% had Grade 3 nausea.
- The most common adverse events were headache, 8% had Grade 3 headache.
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Conclusions

- In this interim analysis of the telaprevir early access program for patients with severe fibrosis or compensated cirrhosis, 80% had HCV RNA <800,000 IU/mL, 45% had HCV <50, 50% had HCV <100 copies/mL, and 40% had undetectable HCV RNA.
- A total of 84% of patients had HCV RNA <50 IU/mL, undetectable at Week 12 (Table 3).
- Of the 102 patients randomized, 81 (80%) had HCV RNA <25 IU/mL undetectable at Week 12 (Table 3).
- Treatment was well tolerated in patients continuing on telaprevir treatment. The most common adverse events were rash, 3% developed Grade 3 rash (all cause, 2% discontinued treatment) and 1% developed Grade 3 rash (all cause, 2% discontinued treatment).

References


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The authors have the following conflicts of interest to declare:

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Table 2. Discontinuation of Telaprevir Due to Adverse Events by Grade

Table 3. Antiviral Therapy: Anti-encephalitic and Blood Substrate, VII. Nucleotide

Table 4. Concomitant Antiretroviral Therapy (ITT; N=102)

Table 5. Grade 2-4 Adverse Events by Grade and Number of Patients (N=102)

Table 6. Concomitant Antiretroviral Therapy: Anti-encephalitic and Blood Substrate, VII. Nucleotide

Figure 3. Baseline Characteristics: Prior Response (ITT; N=102)

Figure 4. HCV RNA ≤25 IU/mL (Detectable and Undetectable) at Week 4 and 12: Main Subgroups.

Figure 5. Outcome of Treatment at Week 12, by Prior Treatment.

Figure 6. Summary of Rash and Anemia (SSC) by Grade.

Figure 7. Percentage of Patients with HIV RNA ≤50 copies/mL.

Figure 8. Worst Treatment-emergent Laboratory Toxicity Grade.

Figure 9. Changes from Baseline in Mean (Standard Error Range) CD4 Count Over Time.