Wirelessly Observed Therapy with a Digital Medicines Program to Optimize Adherence and Target Interventions for Oral Hepatitis C Treatment

Background

• Adherence to hepatitis C virus (HCV) therapy is essential to achieve sustained virologic response (SVR) or cure. Real-world data on adherence with new direct-acting agents to treat chronic HCV are limited, and suboptimal adherence can lead to unnecessary treatment failure. The adherence rates required to achieve SVR are unknown.
• Risk factors for poor adherence include unemployment, lack of education, alcohol/drug use, and psychiatric conditions. Usual methods to measure adherence are inaccurate and do not allow the patient or provider opportunity to respond quickly to perceived nonadherence.
• A novel digital medicine program (DMP), Proteus Discover® captures medication ingestion, providing objective adherence data to allow patients, caregivers, and pharmacists to intervene immediately and ensure medication compliance. DMP includes medications with ingestible sensors, a wearable patch recording physiology and ingestion data, a mobile app, and provider portal.

Objective

• To evaluate real-world adherence in HCV-infected patients treated with sofosbuvir/ledipasvir (SOF/LDV) and using the DMP.
• To evaluate other outcomes, including medical interventions, virologic outcomes, patient satisfaction, and safety of the DMP.

Methods

Study Design

• This was a single-arm, prospective, open-label, IRB-approved, pilot study completed at 2 sites.
• The subjects in the study used the DMP for the duration of their HCV treatment. The DMP consists of these components that function together:
  1. SOF/LDV tablets that are re-packaged with FDA-approved ingestible sensors by a specialty pharmacy. Upon ingestion, the sensor emits a brief signal to the patch before passing through the body naturally.
  2. A wearable sensor patch that collects timestamped digital medication ingestion events and physiologic metrics such as, steps, heart rate and other metrics.
  3. Software that calculates and summarizes adherence patterns, physical activity, rest, and other self-entered data that patients can view through a mobile device, and providers can view through a secure web portal.

Proteus Discover®, a Digital Medicine Program (DMP)

Baseline Demographics and Characteristics

<table>
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<tr>
<th>Total Number of Subjects (N)</th>
<th>28</th>
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<tbody>
<tr>
<td>Male, n (%)</td>
<td>17 (61)</td>
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</table>
| Age, mean years ± SD          | 59 ± 7(|)
| Genotype, n (%)               | 1a | 25 (89) |
|                               | 1b | 3 (11) |
| Race, n (%)                   | Caucasian | 11 (39) |
|                               | African American | 10 (36) |
|                               | Hispanic/Latino | 4 (14) |
|                               | American Indian/Alaska Native and others | 3 (11) |
| Cirrhosis, n (%)              | 1 (4) |
| Prior Treatment History, n (%)| Treatment naive | 26 (93) |
|                               | Previous treatment relapse | 2 (7) |
| Frequency of Mobile Phone Use, n (%) | <1x per week | 3 (11) |
|                               | 2-4x per week | 4 (14) |
|                               | 5x+ per week | 21 (75) |
| Education Level, n (%)        | Less than high school | 7 (25) |
|                               | Some high school/ high school graduate | 12 (43) |
|                               | Some college or college graduate | 15 (46) |
|                               | Post-graduate education | 1 (4) |
| Income Level, n (%)           | <$25,000 per year | 23 (82) |
|                               | ≥$25,000 per year | 5 (18) |
| Psychiatric comorbidity, n (%)| 13 (46) |
| Prior or Current Drug Abuse History, n (%) | 9 (32) |

Adherence Findings

• Patients were connected to the DMP for 93% of expected days (2838 cumulative days).
• 89% of patients were ≥95% adherent to therapy if patient was ≥90% adherent.
• Mean ingestion adherence (DMP measured) was 59%.
• Providers used the DMP data for timely adherence counseling in 39% of patients.

Virologic Findings

• All patients for which data was available (n=21) achieved EOT response.
• 26 patients achieved SVR12, including 2 patients who previously failed therapy; 2 patients relapsed (one with documented suboptimal adherence of <90% and the other with adherence >95%).

Safety Findings

• Four non-serious device-related adverse events (AEs) were reported in 4 patients during the study.
• These AEs of rash and pruritis, which are consistent with the use of a medical adhesive as part of the wearable sensor, and have been resolved.

Primary Endpoint: Percent of subjects with > 95% adherence

Secondary Endpoints:

• Mean ingestion adherence during HCV treatment
• Provider medication decisions made based on information provided by DMP
• Percent of subjects achieving end-of-treatment response (EOT)
• Percent of subjects achieving SVR12+ (at least 12 weeks post-treatment)
• Subject satisfaction survey scores to evaluate subject satisfaction with DMP
• Safety of DMP

Conclusions

• Patients were connected to the DMP 92% of the time, indicating that the system was easy to use even in those patients with low mobile phone use.
• The DMP had a favorable safety profile and provided data to facilitate timely interventions in patients with nonadherence.
• High adherence rates were observed, even in those with risk factors for poor adherence.
• These data suggest that the DMP can support adherence to therapy, reduce unnecessary medication wastage, and optimize SVR rates, including in patients who have previously failed therapy.

References


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