Real World Analysis of ledipasvir/sofosbuvir (Harvoni®) Therapy Completion Rates and Members Achieving Sustained Virologic Response

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Background

- Hepatitis C therapy completion is crucial for cure and members can opt for coordinated benefit coverage, financial assistance and integrated care management through a specialty pharmacy to optimize their outcomes.
- Previous research has demonstrated hepatitis C members exposed to patient specific interventions through specialty pharmacy services had increased adherence and hepatitis C sustained virologic response (SVR) rates (i.e., cure rate) compared to those not using a specialty pharmacy.[1]
- Clinical trial data has found hepatitis C virus infection treatment, which generally includes several drugs with different mechanisms of action, results in high cure rates; however, real world data is lacking.
- In 2016, Baron and colleagues examined patient response to sofosbuvir-based treatment regimens and found the post treatment response was 88 percent (95 percent confidence interval, 84 percent to 93 percent).[2] However, the analysis did not evaluate hepatitis C cure rates using SVR at 12 weeks.
- In addition to documenting treatment cure rates, hepatitis C SVR data obtained from providers could be useful for negotiating care centered contracts for ledipasvir/sofosbuvir treatment failure rates that exceed the SVR rates reported in ledipasvir/sofosbuvir prescribing information.
- There is a paucity of data examining how often hepatitis C laboratory testing data is collected and the real world rates of hepatitis C cure.

Figure 1. Flow of Members in Analysis

976 unique members identified by the specialty pharmacy between November 2014 and February 2016 as receiving hepatitis C care management

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969 (99.3%) of 976 members with a final paid hepatitis C claim

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641 (66.2%) of 969 members with a hepatitis C sustained virologic response laboratory result and corresponding date

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520 (81.1%) of 641 members with ledipasvir/sofosbuvir (Harvoni®) claims

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492 (94.6%) of 520 had their first ledipasvir/sofosbuvir claim on or after April 1, 2015

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317 (64.4%) of 492 members with a sustained virologic response laboratory result 12 to 24 weeks after ledipasvir/sofosbuvir therapy completion

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311 (98.1%) of 317 members receiving at least 8 weeks of ledipasvir/sofosbuvir therapy

Objective

- To examine the real world hepatitis C SVR rate among commercially insured members completing at least eight weeks of ledipasvir/sofosbuvir therapy.

Methods

- Hepatitis C members receiving specialty pharmacy drug management through one specialty pharmacy from November 2014 through February 2016 were eligible for the analysis.
- Administrative pharmacy claims were queried for ledipasvir/sofosbuvir claims among members identified by the specialty pharmacy. A member could have had treatment with other hepatitis C therapies during the time of the analysis.
- Ledipasvir/sofosbuvir length of therapy was based on the number of days of ledipasvir/sofosbuvir supply in the members' claims history and members were required to complete at least eight weeks of therapy to be included in the analysis.
- If a member had at least 56 days (eight or more weeks) of therapy they were considered a completer. Members with 90 or more days without ledipasvir/sofosbuvir following a claim (e.g., only 28 days total), were considered non-completers and excluded from the SVR analysis (N = 6).
- Members were required to have their first ledipasvir/sofosbuvir on or after April 1, 2015.
- Hepatitis C SVR laboratory data results obtained voluntarily from the prescriber via the specialty pharmacy request, when available, was merged with member level ledipasvir/sofosbuvir administrative pharmacy claims data to evaluate SVR "cure rates."
- To determine hepatitis C cure, members were required to have an SVR laboratory test completed between 12 and 24 weeks following ledipasvir/sofosbuvir therapy completion.
- To determine the time between the completion of therapy and the hepatitis C SVR laboratory test date, we used the date of service on the last claim and added the days supply.
  - ⇢ Ledipasvir/sofosbuvir therapy date complete = last date of service plus days supply
- The therapy completion date was subtracted from the date provided for the viral load test from the specialty pharmacy file. Not all hepatitis C SVR laboratory test results included a date.
  - ⇢ Weeks from completion = (SVR laboratory test date minus date complete) divided by seven
- According to ledipasvir/sofosbuvir prescribing information, sustained virologic response (SVR12) was the primary endpoint and was defined as hepatitis C RNA less than Lower Limit of Quantification (LLOQ) at 12 weeks after the cessation of treatment.
  - ⇢ For the members in this analysis, information on the type of test used was not available.
  - ⇢ There were no members with a hepatitis C SVR laboratory test result between 15 and 25 international units (IU) per ml among the 317 members in the final analysis.
  - ⇢ Based on the distribution of hepatitis C SVR laboratory test results, the decision was made to consider a cure at a hepatitis C viral load result of 15 or less.
- SVR rates were reported by the number of weeks of ledipasvir/sofosbuvir therapy completed.

Table 1. Distribution of Members by Hepatitis C Sustained Virologic Response Laboratory Test Result and Date Received by the Specialty Pharmacy

	Members (N = 969)	%
Hepatitis C SVR laboratory test date and SVR result	641	66.2
No hepatitis C SVR laboratory test date but had reported SVR result	156	16.1
No hepatitis C SVR laboratory test date or SVR result	148	15.3
Hepatitis C SVR laboratory test date but no SVR result	24	2.5

SVR = sustained virologic response

Not all totals sum to 100 due to rounding.

Table 2. Distribution of Members Utilizing ledipasvir/sofosbuvir (Harvoni®) by Timing of Hepatitis C Sustained Virologic Response Laboratory Test Result

Lab date findings	Members (N = 492)	%
Hepatitis C SVR laboratory test done between 12 and 24 weeks after ledipasvir/sofosbuvir therapy completion	317	64.4
Hepatitis C SVR laboratory test date came prior to 12 weeks after ledipasvir/sofosbuvir therapy completion	173	35.2
Hepatitis C SVR laboratory test beyond 24 weeks after ledipasvir/sofosbuvir therapy completion	2	0.4

SVR = sustained virologic response

Table 3. Sustained Virologic Response Rates by Weeks of ledipasvir/sofosbuvir (Harvoni®) Therapy Among 311 Members Receiving ≥ 8 Weeks Therapy

Weeks of therapy	% members with SVR <15 IU/mL (N = 311)	Rate of SVR12 reported in clinical trials[3]
8 weeks (56 days)	94% (77/82)	94%
12 weeks (84 days)	98% (187/191)	96 – 99%
More than 12 weeks (range of 112 to 196 days)	97% (37/38)	96 – 99%

SVR12 = sustained virologic response at 12 weeks post treatment

IU = International units

Results

- **Figure 1** shows the flow of members included in the analysis.
  - ⇢ 976 members received hepatitis C specialty pharmacy drug management from November 2014 through February 2016 through one specialty pharmacy.
  - ⇢ 969 (99.3%) of 976 members with a final paid hepatitis C claim.
  - ⇢ 641 (66.2 percent) members had SVR laboratory data, test result and date, available. **(Table 1)**
  - ⇢ 520 (81.1 percent) of the 641 members used ledipasvir/sofosbuvir therapy for their hepatitis C therapy.
  - ⇢ Of the 520 members with ledipasvir/sofosbuvir claims, 28 (5.4 percent) members' first claim was prior to April 1, 2015, and they were excluded from the analysis.
  - ⇢ 492 members had their first ledipasvir/sofosbuvir claim on or after April 1, 2015.
    - – 175 with a hepatitis C SVR laboratory test date outside of range required for analysis.
  - ⇢ 317 ledipasvir/sofosbuvir utilizing members eligible for SVR analysis based on SVR laboratory test result and date occurring between 12 and 24 weeks following completion of ledipasvir/sofosbuvir therapy. **(Table 2)**
  - ⇢ 311 of the 317 members completed at least 8 weeks of ledipasvir/sofosbuvir therapy.

Cure Rates

- 301 (96.8 percent) of the 311 members had a hepatitis C SVR value of 15 or less indicating hepatitis C cure and 10 members had a hepatitis C SVR greater than 15 indicating active hepatitis C virus infection.
- As shown in **Table 3**, the distribution of SVR rates by ledipasvir/sofosbuvir therapy duration were:
  - ⇢ 8 weeks (56 days) – 94 percent achieved SVR 15 or less (77 of 82 members)
  - ⇢ 12 weeks (84 days) – 98 percent achieved SVR 15 or less (187 of 191 members)
  - ⇢ More than 12 weeks (range of 112 to 196 days) – 97 percent achieved SVR 15 or less (37 of 38 members)

Conclusions

- The 97 percent hepatitis C SVR cure rates found in this real world analysis of members receiving specialty pharmacy drug management are equivalent to those reported in clinical trials.
- With one-third of individuals hepatitis C SVR laboratory results not being voluntarily reported to the specialty pharmacy providing care, further assessment is required to identify alternative processes to ensure individuals completing their hepatitis C virus treatment are cured.
- Health insurers should consider implementing care centered contracts focused on hepatitis C cure rates based on SVR laboratory data to ensure members are receiving optimal hepatitis C care.

Limitations

- Data are limited to commercial populations from one specialty pharmacy in the United States; therefore findings may not be generalizable to all pharmacies or Medicare/Medicaid populations.
- Hepatitis C SVR laboratory data is not required to be reported to a health insurer or pharmacy benefit manager. The hepatitis C cure rates in the current analysis likely underestimate the actual SVR rates occurring because of the unknown success rate among individuals without an SVR value.
- Individuals using a specialty pharmacy may be systematically different than those using another channel to receive hepatitis C drug therapy resulting in these findings potentially being non-representative of all hepatitis C treated individuals.
- This study was limited to individuals completing at least eight weeks of therapy and is not representative of all individuals initiated on therapy (i.e., intent to treat analysis). The results therefore are biased in favor of higher SVR rates. However, five of the six members who had less than eight weeks of therapy had an SVR indicating cure.
- There was no comparison group of members who did not receive specialty pharmacy services so results should be considered descriptive.

References

1. AHRQ Pub. No. 13-EHC009-1 December 2012
2. Baron J *et al.* Am Health Drug Benefits. 2016;9(6):327-335.
3. Harvoni® [package insert]. Gilead Sciences, Inc., Foster City, CA; 2016.

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