Analysis of "Real World" Sovaldi® (sofosbuvir) Use and Discontinuation Rates

September 2014

Troyen A. Brennan, M.D., Chief Medical Officer, CVS Health; Alan Lotvin, M.D., Executive Vice President, CVS/specialty, CVS Health; William Shrank, M.D., Chief Scientific Officer, CVS Health

Background

Sovaldi® (sofosbuvir), a new treatment for Hepatitis C manufactured by Gilead, was launched on December 9, 2013 and immediately generated an intense public debate about cost and value in health care. The medication represents an extraordinary clinical breakthrough; in clinical trials, more than 95 percent of patients with Hepatitis C experience sustained viral response, essentially a cure, compared with the 40 percent cure rate observed with prior interferon-based therapies. Treatment tolerability was a main driver of the stunning improvement in the cure rate, as only two percent of patients discontinued therapy during the trial. Substantially higher discontinuation rates have been observed among patients who used previous Hepatitis C therapies.

Sovaldi is very costly, with a list price (Average Wholesale Price) of approximately $1,000 a pill and $84,000 for a 12-week course. More than three million Americans either have Hepatitis C-caused liver disease or are carriers of the disease, highlighting the enormous possible cost of treating this condition in the U.S. This extraordinary cost has stressed commercial, state and federal budgets. While the drug is extremely effective and may offer value in terms of reducing downstream costs, the short-term monetary outlays are considerable and were largely unexpected. The costs have led to an outcry from payors and policymakers, and resulted in widespread debates about the "fairness" of the medication's pricing.

The debate about Sovaldi's efficacy, price, and value has largely been based on the current price of the medication and the results of several clinical trials. The impressive clinical trial results rely on patients' adherence to the medication, and such adherence is often not replicated in real world settings where patients are not observed as closely and where patients are often sicker, older, or more complex than those participating in clinical trials.

To date, little evidence has been presented publicly that assesses Sovaldi adherence and therapy completion rates in real world populations. Similarly, we know little about correlates of therapy discontinuation. Specifically, there is little evidence to suggest whether patients who were previously treated for Hepatitis C and failed therapy (presumably sicker patients) are more likely to complete therapy than those who are naïve to therapy. We are also unaware of any studies of the relationship between the site of delivery of Sovaldi and rates of adherence to therapy. In this White Paper we present real-world evidence about trends in Sovaldi use, rates of therapy discontinuation, and correlates of non-adherence to treatment. We also discuss expected trends as new products become available in the marketplace.

Sovaldi Use
In the nearly nine months since Sovaldi's release, 16,560 patients with pharmacy benefits through CVS/caremark filled prescriptions for the medication. More than 65 percent of the Sovaldi regimens prescribed have been interferon-free (Table 1).

Table 1. Utilization of Sovaldi and the Regimens Used

DRUG UTILIZATION (# OF MEMBERS)*	BOOK OF BUSINESS	
	N	%
Sovaldi (sofosbuvir)	16,560	76%
Olysio (simeprevir)	5,194	24%
Total	21,754	100%
Sovaldi utilization in combination with other drugs		
Sovaldi + ribavirin ONLY	7,070	43%
Sovaldi + ribavarin + pegylated interferon	5,599	34%
Sovaldi + Olysio ONLY	3,772	23%
Total	16,441	100%

*Results bases on paid claims data

Discontinuation Rates and Correlates of Discontinuation
To study discontinuation rates, we created a cohort of patients who were continuously eligible with CVS/caremark insurance for 44 months in order to establish previous use of any Hepatitis C regimen. We identified all patients who were continuously eligible and started a Hepatitis C regimen with Sovaldi on or before 5/15/14 in order to assess rates of discontinuation or completion of the regimen. A total of 1,965 patients met this eligibility criteria.

Among those patients who began Sovaldi in combination with other medications, Sovaldi discontinuation rates were approximately four times greater than the rates observed in clinical trials (Table 2): Sovaldi+Peg-IFN+RBV (10.2 percent of patients discontinued), Sovaldi+Olysio (4.2 percent), and Sovaldi+RBV (9.0 percent). Across regimens, treatment-naïve patients were 64 percent more likely to discontinue therapy with Sovaldi than treatment-experienced patients: 8.7 percent treatment-naïve patients discontinued therapy vs. 5.3 percent for treatment-experienced patients ($p<0.05$).

Table 2: Discontinuation Rates, by Regimen

	N Utilizer*	N Treatment Competed	%	N Treatment Discontinued†	%	Discontinuation Rates in Clinical
Sovaldi+PegIFN/RBV	738	663	89.8%	75	10.2%	2.0%
Treatment-experienced‡	145	134	92.4%	11	7.6%	
Treatment-naïve§	593	529	89.2%	64	10.8%	
Sovaldi+Olysio	547	524	95.8%	23	4.2%	3.6%
Treatment-experienced	115	112	97.4%	3	2.6%	
Treatment-naïve	432	412	95.4%	20	4.6%	
Sovaldi+RBV	680	619	91.0%	61	9.0%	0–2.0%
Treatment-experienced	97	92	94.8%	5	5.2%	
Treatment-naïve	583	527	90.4%	56	9.6%	
All Sovaldi regimens[1]	1,965	1,806	91.9%	159	8.1%	
Treatment-experienced	357	338	94.7%	19	5.3%	
Treatment-naïve	1,608	1,468	91.3%	140	8.7%	

*Members who initiated therapy between 12/1/2013 and 5/15/2014, with paid claims and continuous eligibility between 1/1/2011 and 8/24/2014.

†Patients who had refill gaps exceeding the allowable gap period of 15 days were classified as discontinuers.

‡Patients who were treated with a Hepatitis C drug between 1/1/2011 and 11/30/2013

§Patients who were not treated with a Hepatitis C drug between 1/1/2011 and 11/30/2013

[1]Treatment-experienced vs. Treatment-naïve; $p<0.05$.

Discontinuation rates also varied by the site of delivery. We evaluated discontinuation rates in the CVS Health organization, where specialty patients receive the same counseling and ongoing patient-centered support services from central specialists whether they access their medications through home delivery or at CVS/pharmacy retail stores through our Specialty Connect™ program. We compared discontinuation rates for patients who filled Sovaldi regimens in CVS/pharmacy retail locations or CVS/caremark specialty pharmacies with patients who filled in non-CVS Health-related outlets. To conduct this analysis, we included members who initiated therapy between 12/1/2013 and 5/15/2014, with paid claims and continuous eligibility between 12/1/2013 and 8/24/2014

In general, discontinuation rates were considerably higher in non-CVS Health outlets. When patients filled their Sovaldi regimens at either CVS/pharmacy retail stores or CVS/caremark specialty pharmacies, through the Specialty Connect™ program, they discontinued their regimens 5.9 percent of the time. Patients who filled outside of CVS Health discontinued 8.5 percent of the time, a 44 percent increased rate of discontinuation compared with CVS Health sites. Discontinuation rates were 8.8 percent for non-CVS/pharmacy retail locations and 8.3 percent for non-CVS/caremark specialty pharmacies. (Table 3)

Table 3: Discontinuation Rates, by Delivery Channel, Within CVS/caremark Beneficiaries

REGIMEN	PHARMACY CHANNEL	MEMBERS*	TREATMENT DISCONTINUATION BEFORE 12 WEEKS†, N(%)
Sovaldi + PegIFN/RBV	CVS/caremark specialty pharmacy**	1,171	85 (7.3%)
	Non-CVS/caremark specialty pharmacy‡	731	73 (10.0%)
	-Retail	572	*63 (11.0%)*
	-Specialty	129	*9 (7.0%)*
Sovaldi + Olysio	CVS/caremark specialty pharmacy**	768	35 (4.6%)
	Non-CVS/caremark specialty pharmacy‡	552	43 (7.8%)
	-Retail	389	*31 (8.0%)*
	-Specialty	146	*11 (7.5%)*
Sovaldi + RBV	CVS/caremark specialty pharmacy**	1,096	60 (5.5%)
	Non-CVS/caremark specialty pharmacy‡	767	59 (7.7%)
	-Retail	589	*43 (7.3%)*
	-Specialty	133	*14 (10.5%)*
All Sovaldi Regimens[1]	CVS/caremark specialty pharmacy**	3,035	180 (5.9%)
	Non-CVS/caremark specialty pharmacy‡	2,050	175 (8.5%)
	-Retail	1,550	137 (8.8%)
	-Specialty	408	34 (8.3%)

Sovaldi and Olysio launched on December 9, 2013

*Members who initiated therapy between 12/1/2013 and 5/15/2014, with paid claims and continuous eligibility between 12/1/2013 and 8/24/2014.

**Includes both CVS/caremark specialty pharmacy and CVS/pharmacy retail locations through the Specialty Connect program

†Patients who had refill gaps exceeding the allowable gap period of 15 days were classified as discontinuers.

‡ Includes "other" sites: home infusion therapy provider, long term care, and institutional pharmacies

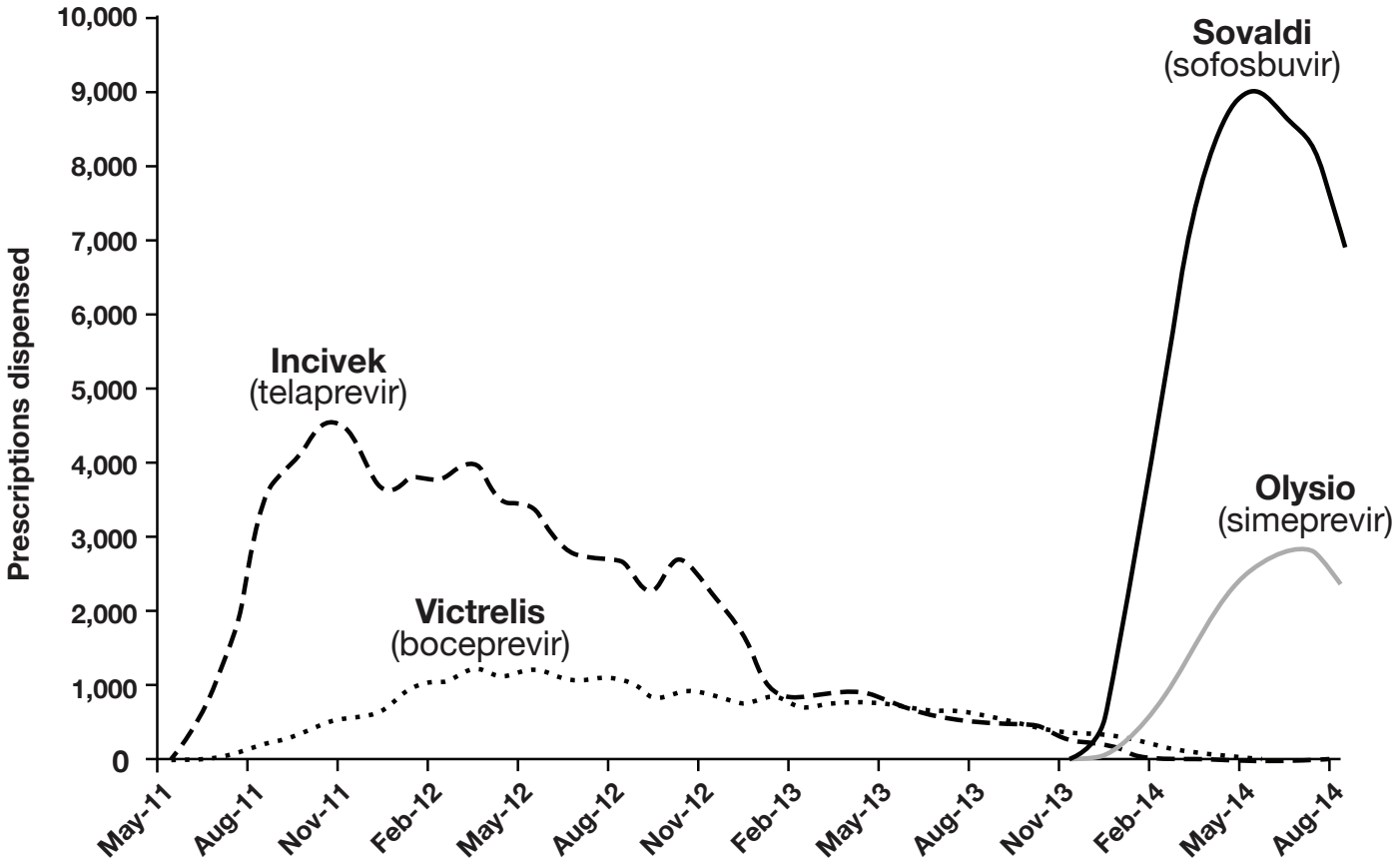
[1]CVS/caremark specialty pharmacy vs. non-CVS/caremark specialty pharmacy; $p<0.001$

The analysis did not adjust for benefit plan design which may provide different incentives for members to complete treatment.

Current and Future Utilization

The practice of "warehousing" patients, waiting to treat until new and improved therapy becomes available, has a rich history in Hepatitis C. In reviewing utilization data over the last four years, it is clear that hepatologists employed an elective approach to the timing of initiation of therapy for those patients without severe sequelae from Hepatitis C. In 2011, when Incivek® (telaprevir) and Victrelis® (boceprevir) were approved for the treatment of Hepatitis C, they represented an important improvement in the ability to treat the disease. As illustrated in Figure 1 below, when these drugs became available in May of 2011 there was a rapid peak in utilization which dissipated when news of the pending availability of a new and improved therapy, Sovaldi, began to circulate. Considering that approximately half of those with Hepatitis C are carriers and unaware they have the disease (approximately 1.5 million Americans) and that the majority of the 1.5 million Americans who are diagnosed with the disease have little or no symptoms, experts suggest that these patterns of peaked use when improved treatments become available will continue.

Figure 1: Utilization Trends of Hepatitis C Treatments (May 2011 – Aug 2014)



Beginning December 2013, when Sovaldi first became available, there was a massive rush to use the medication, with increasing numbers of patients beginning treatment each month (Figure 1). This was due to the fact that in the months leading up to the Food and Drug Administration's approval of Sovaldi, many patients with Hepatitis C who were not experiencing symptoms or adverse health effects had delayed pursuing any treatment until the new, highly effective drug became available. In contrast to the rapid uptake observed initially, CVS Health data show a plateau and then a downward trend in the number of new starters of Sovaldi during May – August 2014.

Experts anticipate another substantial uptick in use in late September or October 2014, when Gilead, the manufacturer of Sovaldi, releases a new regimen for Hepatitis C that combines Sovaldi and ledipasvir into a single pill that is taken once a day. This regimen confers similar efficacy to multi-pill regimens and requires only an 8-week course of therapy compared with Sovaldi's current 12-week course. Experts believe that many hepatologists have been waiting for the release of this new single pill regimen and will initiate therapy for lower acuity patients when this medication becomes available. The pharmaceutical manufacturer Abbvie plans to release a similar all oral regimen at nearly the same time. The simplicity of these options may further reduce treatment discontinuation rates, although this cannot be determined at present. Additional peaks in use may be seen several months later, when new products from other manufacturers become available, which is likely to drive down costs.

Conclusions

CVS Health followed 1,965 patients who began Sovaldi to treat Hepatitis C during December 2013 – Aug 2014. We found that 8.1% of patients discontinued the drug during the recommended 12-week course, approximately a 4-fold increase in the discontinuation rates observed in clinical trials. Patients with less advanced Hepatitis C disease (those naïve to therapy) were markedly less likely to complete treatment than those who had previously received other Hepatitis C therapies. These findings underscore the well-recognized fact that real world adherence to medication is often poorer than that observed in clinical trials. It is reassuring to note that discontinuation rates were substantially lower in the CVS/caremark specialty pharmacy, where additional counseling and patient support is provided.

Sovaldi is an effective, curative therapy but also a costly one, and Sovaldi treatment discontinuation represents a substantial cost to the health care system without the corresponding clinical benefit and value. Our data suggest that all patients who receive Sovaldi should be followed closely by their providers to support adherence to therapy. Because treatment-naïve patients with less advanced disease discontinued Sovaldi more often, health care providers may choose to prioritize treatment for those who have more advanced disease. We anticipate upcoming spikes in Sovaldi use as new, simpler, and less expensive regimens become available. By anticipating these spikes in use, payors can augment current strategies to improve appropriate adherence in those who initiate therapy, and plan for the substantial cost outlays that will arise.