Poster
SU1888

Long-term Clinical Value of Telaprevir for Treatment of Treatment-naïve and Treatment-experienced Patients with Hepatitis C Virus Infection: Projections Using Decision-analytic Modeling

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BACKGROUND

- Of the worldwide population, 2% to 3% (130-170 million people) are infected with the hepatitis C virus (HCV), including approximately 3.2 to 3.9 million people in the United States (US).
- Left uncured, HCV can lead to scarring of the liver (i.e., compensated cirrhosis) and progression to liver failure (i.e., advanced liver disease), including decompensated cirrhosis (DCC) and/or hepatocellular carcinoma (HCC).
- The goal of treatment of chronic HCV infection is sustained virologic response (SVR), or viral cure, defined as undetectable HCV RNA 24 weeks after the conclusion of treatment.
- Telaprevir (TVR), in combination with pegylated interferon alfa-2a and ribavirin (PR), has been investigated in phase 3 studies for the treatment of chronic genotype 1 HCV infection.
  - ADVANCE was a randomized, double-blind, placebo-controlled, multicenter trial that compared TVR+PR with PR alone in a treatment-naïve population.[1]
  - REALIZE was a randomized, double-blind, placebo-controlled, multicenter trial that compared TVR+PR with PR alone in a treatment-experienced population composed of three groups of patients with prior PR treatment failure: (1) null responders, (2) partial responders, and (3) relapsers.[2]
- These studies showed that TVR+PR combination therapy resulted in significantly higher SVR rates compared with PR therapy.
  - Up to 75% of treatment-naïve patients achieved SVR with TVR-based therapy.[1]
  - Among treatment-experienced patients, TVR-based therapy resulted in SVR rates three to five times higher than retreatment with PR alone.[2]

OBJECTIVE

- To explore the potential long-term clinical value of TVR-based therapy using a Microsoft Excel-based decision-analytic model.

METHODS

Model Structure

- A two-phase (treatment and post-treatment) Microsoft Excel decision-analytic model was developed to estimate the health outcomes of TVR+PR combination therapy versus PR therapy alone over remaining patient lifetime for parallel hypothetical cohorts of 1,000 genotype 1 HCV patients with initial METAVIR fibrosis scores of F0 through F4 (Figure 1).
- The population analyzed comprised two patient subgroups:
  1. Treatment-naïve patients
  2. Treatment-experienced patients who had prior PR therapy resulting in null response, partial response, or relapse, as defined by guidelines published by the American Association for the Study of Liver Diseases (AASLD).[3]
- First, patients in their respective cohorts moved through the 72-week decision-tree treatment phase of the model that mirrored the clinical trials (Figure 2). For the remainder of patient lifetimes, patients moved through the cyclic Markov-process post-treatment phase of the model (Figure 3).
- In any annual cycle, patients could remain in or transition among the following health states (Figure 3):
  - Four precirrhosis health states (METAVIR fibrosis scores F0-F3)
  - Compensated cirrhosis (METAVIR fibrosis score F4)
  - Decompensated cirrhosis (DCC)
  - Hepatocellular carcinoma (HCC)
  - Liver transplantation (LT)
  - HCV-related death
  - Non-HCV-related death.

Figure 1: Overview of the Model Structure

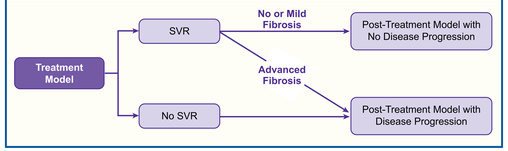
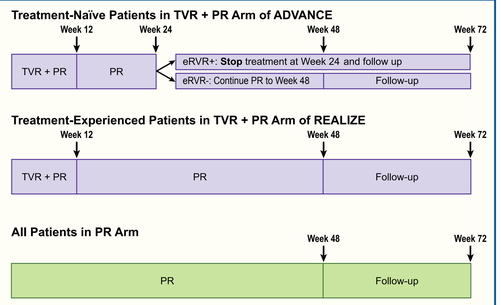
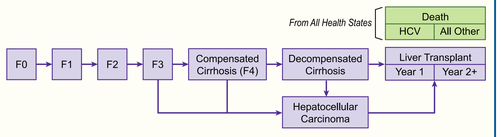


Figure 2. Overview of the Treatment Phase of the Model



eRVR = extended Rapid Virologic Response: undetectable HCV RNA at weeks 4 and 12 of the treatment period.

Figure 3. Overview of Model Health States and Transitions[a]



[a]Transition probabilities between health states were allowed to differ depending on achievement of SVR. In particular, patients with SVR and with no or mild baseline fibrosis (F0-F2) experienced no further liver deterioration.

Input Parameters

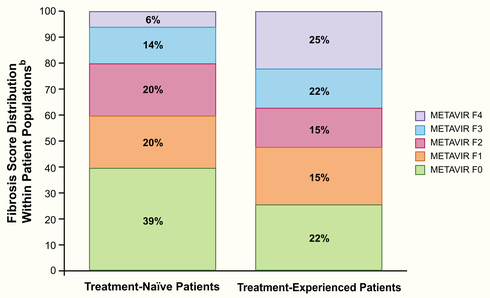
- Clinical data, including patient demographics (age, sex) (Table 1), initial disease severity (METAVIR fibrosis scoring) (Figure 4), and treatment outcomes (attainment of SVR) (Figure 5), were based on results from the TVR phase 3 studies ADVANCE[1] and REALIZE.[2]
- Health-state transition probabilities (i.e., progression in METAVIR fibrosis score and progression to DCC, HCC, and LT) were obtained from the published literature.[4-10]
- Utility scores used for calculation of quality-adjusted life years (QALYs) were derived from patient assessments performed in the TVR phase 3 studies ADVANCE and REALIZE, as well as from the published literature.[11]
  - On-treatment utility scores implicitly accounted for decrements in quality of life that were attributable to adverse events related to treatment regimens.
- Mortality risks were derived from the published literature and US life tables, and included HCV-related death from liver disease as well as death from all other causes.[4,6,7,9,10,12]

Table 1. Initial Demographic Characteristics of Modeled Patients

Model Parameter	Value
Treatment-naïve patients (ADVANCE)	
Median age, years	49
Male, %	59
Treatment-experienced patients (REALIZE)	
Median age, years	51
Male, %	69
Patient distribution,[a] %	
Relapsers	55
Partial responders	18
Null responders	27

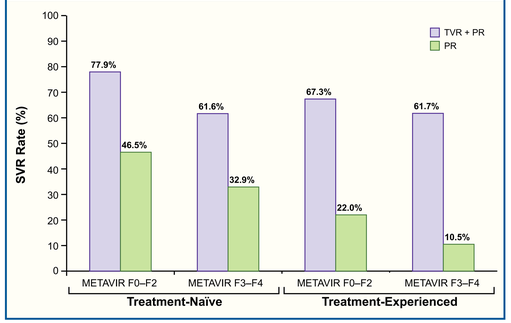
[a]The treatment-experienced population in the REALIZE trial comprised three groups of patients based on type of previous PR treatment failure.

Figure 4. Initial Distribution of Patients in METAVIR Fibrosis Score Health States[a]



[a]Distribution reflects the pooled patient populations from the TVR+PR and PR-Only treatment arms in the clinical trials.
[b]Values in each column do not sum to 100% due to rounding; actual values sum to 100%.

Figure 5. Treatment Efficacy (SVR Rate by Initial METAVIR Fibrosis Score)



RESULTS

- The model estimated that treatment-naïve and treatment-experienced patients who were treated with TVR-based therapy lived an average of 2.0 and 3.4 years longer, respectively, than patients in the PR cohort (Table 2).
- On a quality-adjusted basis, treatment-naïve and treatment-experienced patients who were treated with TVR-based therapy lived an average of 2.4 and 3.8 QALYs longer, respectively, than patients in the PR cohort (Table 2).

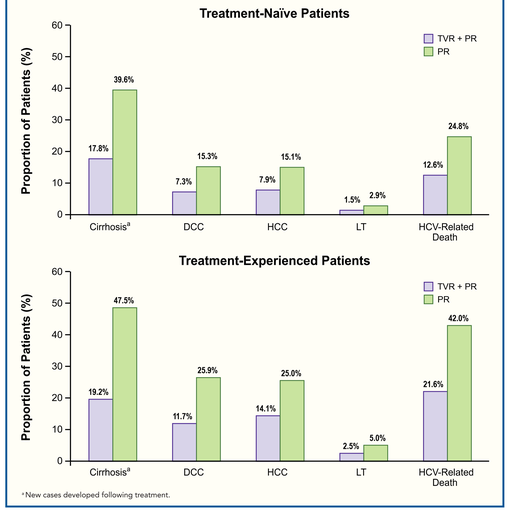
Table 2. Summary of Model Analysis Results: Impact of Treatment on Life Expectancy

	Treatment-naïve		Treatment-experienced	
	TVR+PR	PR	TVR+PR	PR
Life-years accrued[a]	32.4 (20.0)	30.4 (19.2)	26.9 (17.6)	23.5 (16.0)
QALYs accrued[a]	27.6 (17.0)	25.2 (15.9)	22.6 (14.8)	18.8 (12.8)

[a]Discounted values in parentheses; discount rate = 3% per annum.

- Over the course of remaining lifetime, the model projected that patients on TVR-based therapy developed about 50% fewer cases of compensated cirrhosis, DCC, HCC, and LT compared with PR patients (Figure 6).
- The model also projected a nearly 50% reduction in HCV-related death for patients treated with TVR+PR compared with patients treated with PR alone (Figure 6).

Figure 6. Proportion of HCV Infection Patients Who Developed Clinical Outcomes of Interest Over Remaining Lifetime



[a]New cases developed following treatment.

- All results were consistent over a wide range of variations in the model assumptions and input parameter values; the model results were most sensitive to changes in the modeling time horizon (i.e., shorter time horizons than the base-case "lifetime" analysis).

LIMITATIONS

- This analysis involves the typical limitations of pharmacoeconomic analyses (i.e., results reflect inputs and assumptions that were employed in the analysis).
- The model used clinical inputs from the registration trials of TVR, which represent efficacy in a controlled environment rather than in a real-world setting.
- To estimate the long-term impact of clinical trial outcomes, the model projected the course of liver disease for each individual over his or her remaining lifetime based on published disease-progression data.
- The distribution of patient types in prior treatment-experienced groups reflected the patient population studied in the registration trials of TVR.

CONCLUSIONS

- **Our model projected substantial reductions (about 50% overall) in future HCV-related clinical burden in patients with genotype 1 HCV infection who were treated with telaprevir-based therapy compared with peginterferon/ribavirin alone.**
- **Relative reductions in HCV-related clinical burden were similar for treatment-naïve and treatment-experienced patients, indicating that telaprevir-based therapy may have considerable long-term clinical benefits even in hard-to-treat populations.**
- **Given the high costs of treating advanced liver disease caused by HCV infection, there may be substantial economic value associated with the clinical benefits realized by telaprevir-based therapy, which warrants further study on its own.**

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AUTHOR DISCLOSURES

Brogan, Miller, Talbird, and Thompson are current employees of RTI Health Solutions. **Deniz** is a current employee and stock owner of Vertex Pharmaceuticals Incorporated. This research was performed by RTI Health Solutions and funded by Vertex Pharmaceuticals Incorporated.