QUERI

Assessment of Alternative Treatment Strategies for Chronic Genotype 1 Hepatitis C

EXECUTIVE SUMMARY

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

QUERI provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help to:

- develop clinical policies informed by evidence
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge

In 2009, the ESP Coordinating Center was created to expand the capacity of QUERI Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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EXECUTIVE SUMMARY

BACKGROUND

There is great potential to improve health outcomes for Veterans and other patients with chronic genotype 1 (GT1) Hepatitis C (HCV) infections through the use of newly-available triple combination therapies that include directly acting antivirals (DAA) along with recently developed patient genotyping (IL-28B) which is predictive of HCV treatment response. Chronic GT1 HCV infections have been historically difficult to treat, with low cure rates on standard two drug therapy (Pegylated Interferon + Ribavirin), high rates of side-effects and treatment discontinuation, and low rates of uptake. Recently, FDA approved two DAAs (boceprevir and telaprevir). Used in combination with standard two drug therapy as triple therapy, these DAAs show higher rates of sustained viral response, though they are also more costly and have more severe side-effect profiles. IL-28B genotyping can help to identify patients least likely to respond to standard therapy and hence who stand to benefit the most from triple therapy and for whom, therefore, the increased risks of side-effects may be most justified.

METHODS

We addressed four related questions:

- Key Question #1: What are the current usage patterns of directly acting antivirals and of IL-28B patient genotyping in the VA health system? And how do these patterns differ by VISN?
- Key Question #2: What will be the health impacts of using either of two available directly acting antivirals combined with pegylated interferon and ribavirin (triple therapy)?
- Key Question #3: How will be the magnitudes of the health impacts measured in Key Question #2 change if IL-28B patient genotyping is used to offer triple therapy to those less likely to benefit from two-drug pegylated interferon + ribavirin?
- Key Question #4: What will be the cost and resource use patterns when using either triple therapy or IL-28B-guided triple therapy?

We used analysis of observational data and decision analysis to answer these questions over a 5 year time horizon, all in comparison to health outcomes and costs if standard two-drug treatment were continued without adoption of either of the new technologies. Importantly, these results are appropriate for short-term budgeting and planning considerations but are not appropriate for formal cost-effectiveness analyses as they do not represent the full costs and benefits experienced over a life time.

PEER REVIEW

A draft version of this report was reviewed by six technical experts, as well as clinical leadership. Reviewer comments were addressed and our responses were incorporated in the final report (Appendix A)

RESULTS

Key Question #1: What are the current usage patterns of directly acting antivirals and of IL-28B patient genotyping in the VA health system? And how do these patterns differ by VISN?

Between July 2011 and June 2012 nearly 3,000 people initiated DAA treatment, with approximately 80% using on-formulary boceprevir (Boceprevir N=2,366, Telaprevir N=501). During this same period, 2,171 individuals had an IL-28B test. There was heterogeneity in the number of people taking up DAA therapies and IL-28B testing across VISNs.

VISNs differed in their rate of use of IL-28B testing in patients receiving DAAs, with a national average just above 10 percent. VISN 22 had the greatest number of IL-28B tests, while VISNs 8, 16, and 21 had the greatest number of patients initiating DAA therapy. In some VISNs there are more patients initiating DAA therapy than getting IL-28B tests, while in other VISNs the reverse was true. Seven VISNs used testing in five percent or less of patients receiving DAA medications, whereas three VISNs tested 30 percent or more of their patients.

The median length of boceprevir treatments was just under 28 weeks. Of those who initiated boceprevir, 89% continued to 8 weeks, 81% to 12 weeks, 76% to 16 weeks, and 29% to 32 weeks. Telaprevir treatment episodes were much shorter per its therapeutic protocol. The median length of telaprevir treatment was between 12 and 16 weeks. None lasted beyond 28 weeks.

Key Question #2: What will be the health impacts of using either of two available directly acting antivirals combined with pegylated interferon and ribavirin (triple therapy)?

We used simulation modeling analysis over five years to project the likely effect of universal triple therapy compared to standard therapy. Universal triple therapy was likely to reduce the annual number of cases of decompensated cirrhosis by 10-29 (current uptake: 10; doubled uptake: 29; quadrupled uptake: 50), the annual number of cases of hepatocellular carcinoma by 5-16 (current: 5; doubled: 16; quadrupled: 27) and the annual number of liver transplants by 0-1 (current: 0; doubled: 1; quadrupled: 2). Compared to standard therapy, adoption of universal triple therapy is likely to increase the annual number of quality adjusted life years (QALYs) by 148-213 (current: 148; doubled: 213; quadrupled: 322).

Key Question #3: How will the magnitudes of the health impacts measured in Key Question #2 change if IL-28B patient genotyping is used to offer triple therapy to those less likely to benefit from two-drug pegylated interferon + ribavirin?

We used simulation modeling analysis over 5 years to compare IL-28B guided triple therapy to standard two-drug therapy. IL-28B guide triple therapy was likely to reduce the annual

number of cases of decompensated cirrhosis by 8-26 (current uptake: 8; doubled uptake: 26; quadrupled uptake: 45), annual cases of hepatocellular carcinoma by 4-14 (current: 4; doubled: 14; quadrupled: 25), and annual numbers of liver transplants by 0-1 (current: 0; doubled: 1; quadrupled: 2). Compared to standard therapy, IB-28B guided triple therapy is likely to result in an annual increase in QALYs of 110-145 (current: 110; doubled: 145; quadrupled: 225).

Key Question #4: What will be the cost and resource use patterns when using either triple therapy or IL-28B-guided triple therapy?

Based on our simulation modeling analysis, replacement of standard two-drug therapy with triple therapy was likely to increase total expenditures for HCV treatment and care for individuals with GT1 HCV by $32-$100 million annually, depending on treatment strategy and uptake patterns. At the current uptake rate of 2 percent per year, universal triple drug therapy would be expected to cost $43 million more than standard two-drug therapy. IL-28B guided therapy would cost $32 million more.

ABBREVIATIONS TABLE

Abbreviation	Meaning
DAA	Directly Acting Antiviral
DSS	Decision Support System
FDA	U.S. Food and Drug Administration
FY	Fiscal Year
GT1	Genotype 1
HCV	Hepatitis C Virus
IEN	Internal Entry Number
IL-28B	Interleukin 28-B
NDC	National Drug Code
PEG	Pegylated Interferon
QALY	Quality Adjusted Life Year
RIB	Ribavirin
SVR	Sustained Viral Response
VISN	Veterans Integrated Service Network