Boceprevir for Chronic Genotype 1 Hepatitis C Virus in the Current Health Care Setting in Greece: A Cost-effectiveness Analysis

Kostas Athanasakis, PhD[1]; Shannon Allen Ferrante, PhD[2]; Ilias-Ioannis Kyriopoulos, MSc[1]; Ioannis Petrakis, MSc[1]; Mary Hill, MSc[3]; Maria-Pagona Retsa, MSc[3]; and John Kyriopoulos, PhD[1]

[1]Department of Health Economics, National School of Public Health, Athens, Greece; [2]Merck Sharp & Dohme Corporation, Whitehouse Station, New Jersey; and [3]MSD Hellas, Athens, Greece

ABSTRACT

Purpose: Boceprevir, as an add-on to the standard of care (SOC) for chronic genotype 1 hepatitis C virus (G1 HCV), pegylated interferon + ribavirin for 48 weeks (PEG + RBV), has been reported to have a clinical profile superior to that of SOC alone. The objective of the present study was to compare the cost-effectiveness of triple therapy with PEG + RBV + boceprevir to that of SOC in treatment-naive and treatment-experienced patients with G1 HCV in Greece.

Methods: A Markov model that simulated the quality-adjusted life expectancy and corresponding costs of treating G1 HCV infection provided the basis of the analysis. Treatment strategies under consideration were those in the Phase III boceprevir trials: (1) boceprevir response-guided therapy (shortened treatment duration for early responders); (2) fixed-duration (4-week) SOC plus 44 weeks of triple therapy; and (3) 48-week SOC. Efficacy data and the baseline characteristics of the study population were based on data from the SPRINT-2 (Serine Protease Inhibitor Therapy 2) and RESPOND-2 (Retreatment with HCV Serine Protease Inhibitor Boceprevir and PegIntron/Rebetol 2) clinical trials. Health care resource utilization and costs reflect the local clinical setting, with a 3% discount per annum, and were assessed from a third-party payer perspective.

Findings: Triple therapy was projected to reduce liver complications (eg, decompensated cirrhosis, hepatocellular carcinoma, need for liver transplantation, and liver-related death) by 44% to 45% and 49% to 53% in treatment-naive and treatment-experienced patients, respectively, over a lifetime horizon, leading to corresponding gains of 0.87 and 1.25 quality-adjusted life-years gained per patient. Taking into account the costs of medications, treatment, and outcomes management, the estimated incremental cost-effectiveness ratios of triple therapy versus SOC were €10,003 and €10,852 per quality-adjusted life-years gained in treatment-naïve and treatment-experienced patients. Extensive sensitivity analyses suggested that the findings were robust over a wide range of inputs.

Implications: Based on the findings from the present analysis, the addition of boceprevir to PEG + RBV for the treatment of patients with G1 HCV may be a cost-effective alternative in the health care setting in Greece. (*Clin Ther*. 2015;37:1529–1540)

Key words: boceprevir, chronic hepatitis C, cost-effectiveness, genotype 1, pegylated interferon, ribavirin.

INTRODUCTION

Infection with the hepatitis C virus (HCV) is one of the main causes of chronic liver disease worldwide.[1] Chronic HCV infection may result in cirrhosis in up to 20% of cases and is the primary cause of the need for liver transplantation.[2] HCV infection affects an estimated 3% of the world's population, resulting in ~150 million individuals infected with chronic conditions and >350,000 deaths each year due to HCV-related liver disease.[3] The estimated prevalence of HCV in Greece is in the range of 1.5% to 2.0%, with previously undiagnosed cases expected to come about throughout this decade.[4]

There are 2 equally important, yet often contradictory, factors to consider in the management of HCV:

Accepted for publication May 7, 2015.
http://dx.doi.org/10.1016/j.clinthera.2015.05.003
0149-2918/$ - see front matter

(1) the humanitarian burden of the clinical challenges imposed on hepatologists, and (2) the significant impact in terms of health care resource utilization and costs associated with chronic HCV infection. The resulting economic burden is multiplied in cases of advanced liver disease, in which complications due to chronic HCV have been established.[5] A recently published cost-of-illness study from Greece assessed the economic burden of HCV at different stages of the disease.[6] The estimated mean direct cost per patient in those without cirrhosis was €642/y (€1 = US $1.30).[7] Costs related to the management of severe liver disease appeared to increase significantly, ranging from €5934/y[5] in patients with decompensated cirrhosis to >€35,000/y in the first year after liver transplantation.[5]

HCV is a "clever" virus, taking advantage of the host to replicate at 10^{13} new virions per day, resulting in diverse genetic types. So, in addition to the natural selection process, 6 different genotypes exist and have been studied. Genotype 1 (G1) remains the most prevalent worldwide, thus attracting the focus of pharmaceutical development. Recent development in the therapeutic arena of G1 HCV includes the direct-acting antivirals (DAAs)—the protease inhibitors boceprevir and telaprevir—which have been on the EU market since mid-2011. This new era has come about to increase the cure rate in G1 HCV and to modify standard practice in the management of G1 HCV in the health care system in Greece and worldwide.

In view of the significant current and future clinical and economic burdens associated with the dormant chronic infection and the newer therapeutic options already available, the objective of the present study was to assess the cost-effectiveness of triple therapy (pegylated interferon + ribavirin [PEG + RBV] + boceprevir) to that of the standard of care (SOC) (ie, PEG + RBV) in treatment-naive and treatment-experienced patients with G1 HCV in Greece. The setting of interest for the analysis was the third-party payer perspective in Greece, a country under severe financial constraints and deep austerity measures.

MATERIALS AND METHODS

Model Overview

A previously published[7] state-transition Markov model was used for estimating the expected costs and quality-adjusted life-years (QALYs) associated with the treatment strategies being evaluated. The model performed a simulation of the treatment regimens and follow-up period, as well as the clinical course of chronic HCV, to project the lifetime cumulative incidence of advanced liver-related diseases (decompensated cirrhosis, hepatocellular carcinoma) and the need for liver transplantation. The treatment and follow-up periods (maximal duration, 72 wk) were modeled using weekly cycles, whereas the "normal progression" part used a cycle duration of 1 year.

The post-treatment component of the model consisted of 4 health states in those patients who achieved sustained virologic response (SVR) (HCV RNA <25 IU/mL at 24 and 48 weeks) and 10 health states to represent all states of liver disease, as per the current understanding of the disease, in patients who did not achieve SVR (plus an all-cause mortality state). The severity of chronic HCV infection was described by the degree of fibrosis using the Meta-Analysis of Histological Data in Viral Hepatitis scoring system, as follows: no fibrosis (F_0), portal fibrosis without septa (F_1), portal fibrosis with a few septa (F_2), numerous septa without fibrosis (F_3), and compensated cirrhosis (F_4). The progressive-disease model assumed that liver disease in a person with a given fibrosis score may progress to more severe stages or that the patient may remain in that health state. In the absence of successful treatment, regression to less severe health states was not permitted. However, after successful treatment, a patient could achieve SVR, which is considered as cure in patients who are noncirrhotic (Figure 1).

Treatment Alternatives

Treatment strategies under consideration were those in the Phase III boceprevir trials: (1) boceprevir response-guided therapy (shortened treatment duration for early responders); (2) fixed-duration (4-week) SOC plus 44 weeks of triple therapy; and (3) 48-week SOC. In the case of triple therapy, a number of treatment strategies were simulated according to a regimen based on the European labeling of boceprevir[8] and were differentiated according to whether a patient had received HCV treatment at a previous point in time (treatment experienced or treatment naïve) and whether a patient had cirrhosis at the start of treatment.

Triple Therapy

Noncirrhotic Patients

Treatment-Naïve Subgroup. Treatment-naïve patients without cirrhosis received PEG + RBV for 4 weeks,