

## Cost-effectiveness of boceprevir add-on treatment of hepatitis C virus genotype 1 patients in Denmark

Ehlers, Lars Holger; Ferrante, S.; Højsted Kristensen, Malene; Leutscher, Peter; Chhatwal, J.

*Publication date:*  
2013

*Document Version*  
Early version, also known as pre-print

[Link to publication from Aalborg University](#)

### *Citation for published version (APA):*

Ehlers, L. H., Ferrante, S., Højsted Kristensen, M., Leutscher, P., & Chhatwal, J. (2013). *Cost-effectiveness of boceprevir add-on treatment of hepatitis C virus genotype 1 patients in Denmark*. Poster presented at International Society for Pharmacoeconomics and Outcomes Research, Dublin, Ireland.

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

### **Take down policy**

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.

**Ehlers L**<sup>1</sup>, Ferrante S<sup>2</sup>, Kristensen MH<sup>2</sup>, Leutscher PDC<sup>3</sup>, Chhatwal J<sup>4</sup>  
<sup>1</sup>Aalborg University, Aalborg, Denmark, <sup>2</sup>Merck & Co. Inc., North Wales, PA, USA, <sup>3</sup>Aarhus University Hospital, Aarhus, Denmark, <sup>4</sup>University of Pittsburgh, Pittsburgh, PA, USA

### Background

Approximately 170 million people globally are infected by hepatitis C virus (HCV). In 2013, 17 000 patients were estimated to be HCV infected in Denmark. Only half of them have been diagnosed (1). HCV may cause liver cirrhosis and other liver-related complication such as hepatocellular carcinoma (HCC), which is the leading cause of liver transplants in the United States. (2, 3, 4, 5)

Of the six HCV genotypes, genotype 1 is the most common, but also the most difficult to eradicate by therapy (8, 9). In 2011, boceprevir (BOC), one of the first protease inhibitors, was approved for treatment of HCV genotype 1 infection in previously untreated and treated patients.

### Objectives

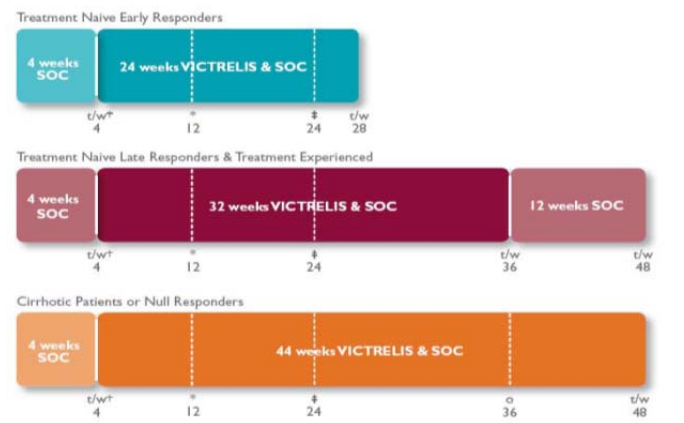
The aim of this study was to evaluate the cost-effectiveness of boceprevir therapy in combination with pegylated interferon plus ribavirin (PEG+R), compared to PEG+R therapy alone, genotype 1 HCV patients, including treatment naïve as well as treatment experienced patients.

### Methods

A Markov model simulating antiviral therapy and disease progression was developed to estimate lifetime healthcare costs and clinical outcomes of alternative treatment strategies. The model simulated the treatment regimens of dual therapy (PEG+R) and triple therapy (PEG+R+BOC), respectively, as recommended in the summary of product characteristics (SPC) and the Danish treatment guidelines. Data on clinical efficacy was taken from phase III clinical trials (SPRINT-2 and RESPOND-2).

The model projected the expected lifetime healthcare costs and clinical outcomes in quality-adjusted life years (QALY). Costs were measured in 2012 Danish kroner (DKK) and clinical outcomes in (QALYs). Both costs and QALYs were discounted at 3 % per year. Incremental cost-effectiveness ratio (ICER) was estimated for treatment naïve and experienced patients in comparison with PEG+R-based therapy. Deterministic and probabilistic sensitivity analyses (PSA) on clinical inputs, costs, health state utility values, and sustained virologic response (SVR) rates were performed to assess the overall decision uncertainty.

Figure 1. Boceprevir treatment duration and futility rules as recommended by SpC



\*futility rules: discontinue all three treatments if patients have HCV\_RNA >= 100 IU/ml at week 12 of detectable viral load week 24. Viral load test week 4 (optional). Addition of boceprevir at start of week 5. For patients with cirrhosis (both treatment naïve and treatment experienced) and historical null responders recommended dosing: - 4 week PR lead in followed by 44 week tri-therapy with boceprevir PEG+ R.

Figure 2 Model Structure



### Model inputs

All patient characteristics were based on information for the Danish database InfCare hepatitis database. (table 1). Treatment related parameters were estimated from SPRINT-2 and RESPOND-2. Information of the probability of receiving liver transplant was estimated from the Nordic liver transplant register (table 2). All health states and treatment related quality of life weights were obtained from previously published studies (table 3). Health state costs were based on previously published studies as well as DRG-tarifs (table 4).

Table 1 Patient characteristic (8)	Untrea	Treated
Gender (%)		
Male	73	73
Female	27	41
Mean age, years (SD)	50 (12)	52 (10)
Race (%)		
Caucasian	99	99
Black	1	1
Baseline METAVIR Score (%)		
F0	24	10
F1	43	27
F2	7	24
F3	6	13
F4	20	27

Table 2 Annual Transition probabilities	Baseline (range)
<b>Fibrosis progression by use of Metavir score</b>	
F0 to F1	0.117 (0.104–0.130)
F1 to F2	0.085 (0.075–0.096)
F2 to F3	0.120 (0.109–0.133)
F3 to F4	0.116 (0.104–0.129)
<b>Cirrhosis progression</b>	
Compensated cirrhosis to decompensated	0.029 (0.010–0.039)
Cirrhosis to HCC (5)	0.028 (0.010–0.079)
Decompensated cirrhosis to HCC (9)	0.068 (0.030–0.083)
<b>Probability of Receiving a Liver Transplant</b>	
Decompensated cirrhosis (10)	0.015 (0.010–0.062)
HCC (10)	0.006 (0-0.04)
<b>Probability of moving from SVR to:</b>	
Decompensated cirrhosis (10)	0.010 (0.002–0.036)
HCC (10)	0.006 (0.002–0.013)
<b>Mortality Rates</b>	
All-cause mortality (11)	age/gender specific
Liver-related mortality associated with	0.182 (0.065–0.190)
Liver-related mortality associated with	0.112 (0.065–0.190)
Liver-related mortality associated with HCC	0.427 (0.330–0.860)
Liver transplant (first year)	0.116 (0.060–0.420)
Liver transplant (subsequent years)	0.044 (0.024–0.110)

Table 3. Utility Weights	Baseline (range)
Baseline utility weights for general	
<b>Anti-viral drug therapy-related</b>	
Peginterferon + ribavirin, no side	0.85 * (baseline fibrosis-stage utility)
Peginterferon + ribavirin +	0.85 * (baseline fibrosis-stage utility)
Anti-Viral-related anemia	(0.83*0.85)*(baseline fibrosis-stage
Post treatment	
Sustained virologic response (cured)	0.83 (0.77–0.90)
Health state utility weights	
F0	0.76 (0.68–0.83)
F1 (14)	0.76 (0.68–0.83)
F2 (14)	0.76 (0.68–0.83)
F3 (14)	0.76 (0.68–0.83)
Compensated cirrhosis	0.74 (0.66–0.83)
Decompensated cirrhosis (first year)	0.66 (0.46–0.86)
Decompensated cirrhosis	0.66 (0.46–0.86)
Hepatocellular carcinoma	0.65 (0.44–0.86)
Liver transplant (first year)	0.69 (0.62–0.77)
Liver transplant (subsequent years)	0.69 (0.62–0.77)
Discount rate	3%

Table 4 Economic Inputs (DKK)	Baseline
<b>Anti-viral drug therapy-related costs (weekly)</b>	
Ribavirin + Peginterferon (15)	2 002
Boceprevir (15)	6 078
Erythropoietin (to treat anemia)	0
Monitoring Costs [1]	239
<b>Health state costs (annual)</b>	
F0 (16)	2 850
F1(16)	2 850
F2 (16)	2 850
F3 (16)	2 850
Compensated cirrhosis (17)	13 600
Decompensated cirrhosis (first year) (17)	47 050
Decompensated cirrhosis (subsequent years) (17)	47 050
Hepatocellular carcinoma (first year) (17)	62 040
Hepatocellular carcinoma (subsequent years) (17)	2 850
Liver transplant (first year) (17)	865 253
Liver transplant (subsequent years) (17)	61 306
Discount Rate for future costs(17)	3%
Time Horizon	Lifetime

### Results

The ICER for PEG+R+BOC therapy versus standard therapy with PEG+R was DKK 241,774 for treatment naïve HCV patients and DKK 98,371 for treatment experienced patients. PSA for treatment naïve patients showed a probability of cost-effectiveness of PEG+R+BOC therapy compared to PEG+R of more than 65 % at a willingness-to-pay threshold of DKK 300,000 (approx. £30,000).

Table 5 Result				
Treatment naïve	Incremental costs	Incremental QALY	ICER's DKK	
Overall BOC vs Peg/R	123,614	0.51	242,380	
F0-F3 BOC vs PEG/R	109,493	0.62	176,602	
F4 BOC vs PEG/R	181,225	0.1	1,812,250	
Treatment experienced				
Overall BOC vs Peg/R	133,271	1.36	97,993	
F0-F3 BOC vs PEG/R	131,333	0.86	152,713	
F4 BOC vs PEG/R	138,638	2.72	50,970	
NR BOC vs PEG/R	145,623	0.87	167,383	

Figure 3 Results of PSA for tr eatment naïve

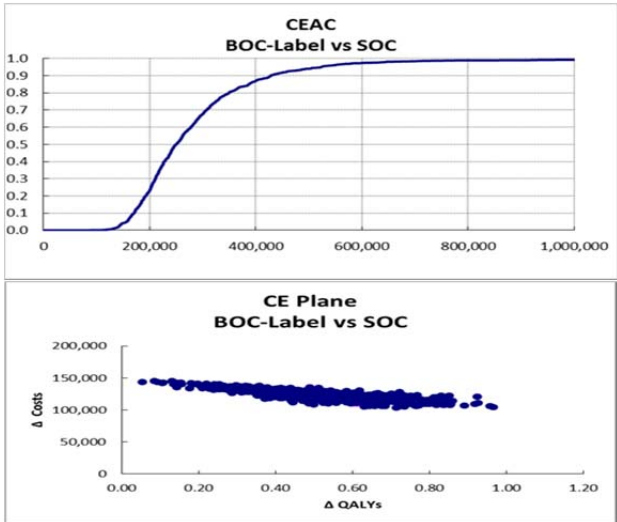
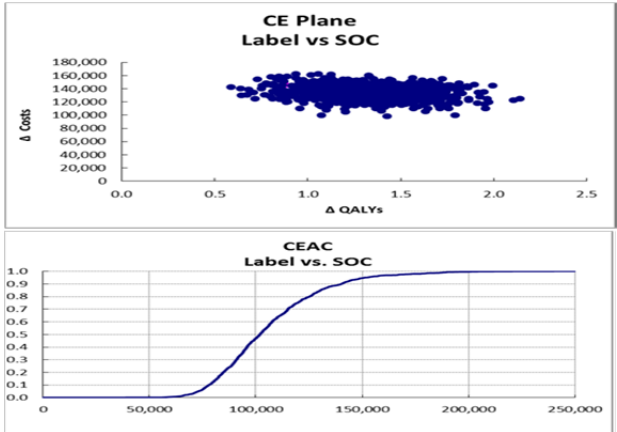


Figure 4: Results for Treatment – Experienced



### Conclusions

From a Danish health economical perspective PEG+R+BOC therapy is cost effective in HCV genotype 1 patients to eradicate virus and to prevent development of late liver manifestations, such as cirrhosis and hepatocellular carcinoma (HCC) irrespectively of previous treatment status. The result was robust to changes in the model as demonstrated by the sensitivity analyses.

### References

- 1) Global burden of human immunodeficiency virus (HIV) and hepatitis B virus (HBV) and hepatitis C virus (HCV) infections: a global perspective. *Lancet Infect Dis*. 2013;13(12):1183-1191.
- 2) The Nordic Liver Transplant Registry. *Am J Transplant*. 2009;9(12):2183-2191.
- 3) Thun H, et al. Estimation of the impact of hepatitis C virus infection on the health care system in Denmark. *Am J Epidemiol*. 2008;167(12):948-954.
- 4) Baruch A, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Gastroenterology*. 1997;112(2):463-472.
- 5) Chaiso A, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2000;32(6):1027-1034.
- 6) Legendre A, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2008;48(2):418-426.
- 7) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 8) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 9) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 10) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 11) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 12) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 13) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 14) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 15) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 16) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 17) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.
- 18) Norder H, et al. Multicenter study of the efficacy and safety of peginterferon alpha-2a plus ribavirin in patients with chronic hepatitis C. *Hepatology*. 2004;40(5):1623-1630.

