Table 1
ICER of each active treatment *vs.* no treatment.

	Cost	QALY	Incremental cost	Incremental QALY	ICER[a]
HBeAg positive pts					
No treatment	83,406	13.69	Reference	Reference	
Telbivudine	90,721	14.96	7315	1.27	5760
Entecavir	90,273	15.21	6867	1.52	4518
Adefovir	91,199	14.68	7793	0.99	**7872**
Lamivudine	87,134	14.67	3728	0.98	3804
Tenofovir	87,615	15.43	4209	1.74	**2419**
HBeAg negative pts					
No treatment	90,866	12.48	Reference	Reference	
Telbivudine	111,097	15.47	20,231	2.99	6766
Entecavir	114,968	16.11	24,102	3.63	6640
Adefovir	103,916	14.21	13,050	1.73	**7543**
Lamivudine	95,547	14.30	4681	1.82	**2572**
Tenofovir	105,889	16.28	15,023	3.8	3953

Bold value represents the higher and lowest value in the group.
Abbreviations: RCT, Randomized Clinical Trial; QALY, Quality Adjusted Life Year; ICER, Incremental Cost-Effectiveness Ratio.
[a] Incremental cost per incremental QALY. All costs are in Euro.

"oral antiviral treatment" on the other side are considered. Ultimately the authors evaluated the efficacy of tenofovir *vs.* all other drugs as the differences between response rates obtained from different trials. However when different treatments are studied in separate trials actual differences between response rates associated with the treatments (treatment effect) are confounded by the differences between the trials (trial effect), thus it is impossible to estimate the effects separately. Typically, trial effects are due to different patients characteristics (e.g. baseline, viral load). With regard to the cost of therapy used in the model it seems that only the cost of drugs was considered without considering the additional cost due to the administration cost, toxicity (e.g. monitoring of renal function for tenofovir) management of side-effects etc. Consequently, the model does not seem sensitive and precise enough for the purpose of comparing active treatments one against the other (see Table 1).

True and appropriate incremental cost per QALY (Quality Adjusted Life Year) gained of each individual oral antiviral therapy compared to "no treatment" can be computed, which are based on the very data of Buti and colleagues [1].

Once this standard approach for computing ICER is used, one can observe that all oral antiviral therapies are cost-effective compared to "no treatment", far below the commonly agreed threshold of 50.000 Euro per QALY. This is reassuring for the decision makers that oral antiviral therapies are value for money, so that the decision on appropriate therapy for the next patient can safely return in the sphere of clinical judgment and physician–patient interaction.

Reference

[1] Buti M, Brosa M, Casado MA, Rueda M, Esteban R. Modeling the cost-effectiveness of different oral antiviral therapies in patients with chronic hepatitis B. J Hepatol 2009;51:640–646.

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Some oral antivirals are more cost-effective than others for the treatment of chronic hepatitis B

To the Editor:

In their letter referring to our study "Modeling the cost-effectiveness of different oral antiviral therapies in patients with chronic hepatitis B", Mantovani and de Portu claim that the presentation of our results is inappropriate. We beg to disagree.

First, the aim of our study, as is stated in the introduction, was to assess the cost-effectiveness of various antiviral drugs [1]. The "no therapy" strategy was included because a considerable number of patients with chronic hepatitis B have their treatment deferred for different reasons. Secondly, as direct comparisons between antiviral treatments are not available then indirect comparison remains the only approach to evaluate cost-effectiveness of any anti-HBV therapy. The limitations of indirect treatment comparisons in cost assessment are well recognized. For this reason, modeling techniques are especially appropriate and indicated to compare the data from different sources [2]. Indeed, modeling techniques allow extrapolation of short/medium-term results from clinical trials to long-term effectiveness outcomes, which is what we did in our model, in line with previous studies [3,4]. In addition, the probabilistic sensitivity analysis helps the reader to better understand eventual differences between the compared options even if the primary data, virological response rates, do not derive from head-to-head studies comparing different antiviral options, as occurs in chronic hepatitis B treatment. The robustness of our model was exhaustively tested in the probabilistic analysis, and the expected variability was analysed within the Monte Carlo simulation. Finally, the basic cost-effectiveness results depicted in Figures 1 and 2 of the manuscript [1] clearly show that a number of treatment options are dominated by others (in some cases by more than one option) [1]. Thus, the only incremental cost-effectiveness ratios (ICERs) to be calculated are those of the more effective options relative to immediately less effective options, performing a standard incremental cost-effectiveness analysis. In our study, ICERs are shown for tenofovir *vs.* lamivudine and no treatment (Table 5 of the manuscript [1]), and the only ICERs omitted are those of lamivudine *vs.* no treatment in both HBeAg-positive and HBeAg-negative patients.

In our opinion, the only real contribution of the letter by Mantovani and de Portu is when they point out that lamivudine is a cost-effective option in relation to "no treatment". This is a well-known fact that has little current relevance, since lamivudine is not a recommended first-line option in the treatment of chronic hepatitis B infection.

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[4] Kanwal F, Gralnek IM, Martin P, Dulai GS, Farid M, Spiegel BM. Treatment alternatives for chronic hepatitis B virus infection: a cost-effectiveness analysis. Ann Intern Med 2005;142:821–831.

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Antiviral therapy for chronic hepatitis B: Challenges in Hong Kong ☆

To the Editor:

I read with great interest the review article by Prof. Liaw published in a recent issue of this journal [1]. The article highlighted the reality and difficulties many patients and clinicians in Asian countries are now facing in the treatment of chronic hepatitis B. Although the more recent antiviral agents (entecavir and tenofovir) have strong antiviral potency and very low risk of drug resistance, these drugs may not be available to all patients in need. This is due to the restricted reimbursement criteria in place in different countries as well as the low income of the population in some areas.

In 2008, the gross national income per capita in Hong Kong was approximately USD 30,380, which was comparable to that of Singapore, Japan, Australia and Europe [1]. Instead of full reimbursement for antiviral drugs, Hong Kong has very restricted criteria of reimbursement. Before July 2008, lamivudine was the only drug reimbursable to patients with significant disease activity while adefovir could only be reimbursed for patients with lamivudine resistance and significant disease activity. After July 2008, lamivudine was not reimbursable to treat new patients. Instead, entecavir could be

☆ HLYC is an advisory board member of Bristol-Myers Squibb, Roche, Novartis Pharmaceutical, Pharmasset and Schering-Plough.