The burden of chronic hepatitis delta in Italy: potential impacts and effects of bulevirtide through Cost of Illness and Cost Consequence Analysis

Poster WED-444

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Conclusions

- The economic burden of HDV infection over 10 years associated with the management and treatment of a hypothetical cohort of 1,000 HDV-RNA positive adult patients with compensated liver disease in Italy in the current scenario without bulevirtide was equal to € 35,117,179
- Compared to the current scenario, the introduction of bulevirtide in the new scenario led to a total expenditure reduction of € 2,032,466. Moreover, the introduction of bulevirtide lead to an increase of 375 (9%) quality-adjusted life years (QALYs) gained and a reduction of 75 (12%) number of deaths in Italy over 10 years

Plain Language Summary

- The hepatitis D virus (HDV) leads to different pathological conditions worldwide, causing the most severe form of viral hepatitis in humans [1]
- The economic impact of HDV infection was estimated through a cost of illness analysis (COI), while the costs and effects of the introduction of bulevirtide for the treatment of chronic HDV were estimated through a cost-consequence analysis (CCA) on a cohort of 1,000 HDV-RNA positive adult patients with compensated liver disease, over a 10-year time horizon
- The total cost of managing patients with HDV in Italy over 10 years is approximately 35 million euros. However, the introduction of bulevirtide led to a saving of 2 million euros, an increase in the number of QALYs and a reduction in the mortality rate
- Despite some limitations, this study can be considered a first attempt to provide an estimate of the total expenditure in terms of both direct and indirect costs for the management of patients with HDV infection in Italy

References: **1**. Yurdaydin C., et al. *J Viral Hepat.* 2010;17(11):749-56. **2**. Stockdale AJ., et al. *J Hepatol.* 2020;73(3):523-32. **3**. European Medicines Agency. Hepcludex [Available from: *https://www.ema.europa.eu/en/medicines/human/EPAR/hepcludex*].

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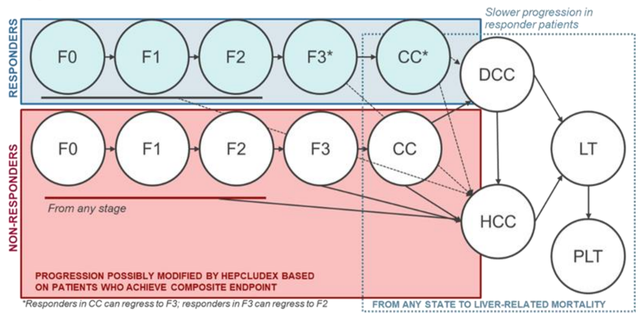
Introduction

- The manifestation of HDV infection can either be acute or result in prolonged, chronic illness. Its advancement can result in liver decompensation, hepatocellular cancer (HCC), and eventually necessitate liver transplantation [2]. New molecular targets have recently been identified for treating HDV; among them, the peptide entry-inhibitor bulevirtide (BLV). In July 2020, BLV 2 mg received conditional marketing authorisation by the EMA for the treatment of CHD, with the recommendation to maintain the treatment until clinical benefit is observed [3]
- The aim of this study was to assess the expenses borne by the National Health Service (NHS) and society due to HDV in Italy and to analyze the costs and impacts of bulevirtide in treating chronic hepatitis D infection among HDV-RNA positive adult patients with compensated liver disease

Methods

- The model was a decision tree followed by a Markov cohort model that follows patients through the lifetime of their disease, based on different state transitions and with a 24-week cycle length (**Figure 1**)

Figure 1. Model structure overview

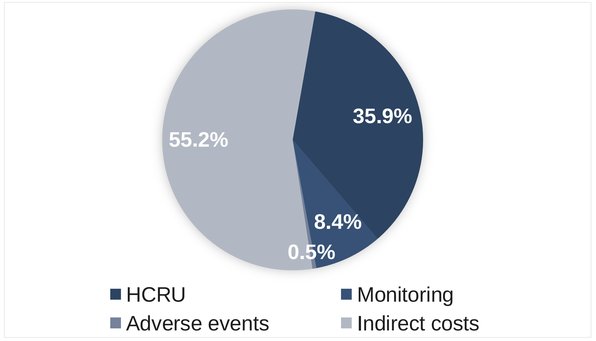


- A cost-of-illness analysis was developed to estimate the economic impact of HDV infection in Italy on a hypothetical cohort of 1,000 HDV-RNA positive adult patients with compensated liver disease and a mean age of 45.0 years. The economic burden of HDV infection was studied over a 10-year time horizon, considering a discount rate of 3.0% for both costs and outcomes across the model
- A cost consequence analysis (CCA) was carried out with the aim of estimating the cost and consequences of using bulevirtide for the treatment of HDV. The most relevant outcomes were QALYs and number of deaths avoided. For the CCA, two scenarios were considered: the first includes PEG-IFN-α and best supportive care (BSC) as the treatment options available in the current clinical practice for HDV patients, while the second introduces the use of bulevirtide.
- The analyses were conducted from the NHS perspective and societal perspective, so direct and indirect costs were considered. Regarding direct costs, the study included Healthcare resource use costs (HCRU), intended as health state costs associated with the management of the disease (including outpatient visits, biochemical analyses, and instrumental procedures), monitoring costs and adverse events costs associated with treatment. Regarding societal perspective, the study considered the loss of patient's productivity caused by HDV infection

Results

- The overall expenditure in the current scenario without bulevirtide was equal to € 35,117,179 (**Table 1**)
- Most of the total expenditure (current scenario) for HDV is allocated between indirect costs (55.2%) and HCRU (35.9%). The costs related to the management of adverse events are minimal, while monitoring costs represent the remaining 8.4% of the total expenditure (**Figure 2**)

Figure 2. Distribution of total HDV expenditure among 1,000 patients

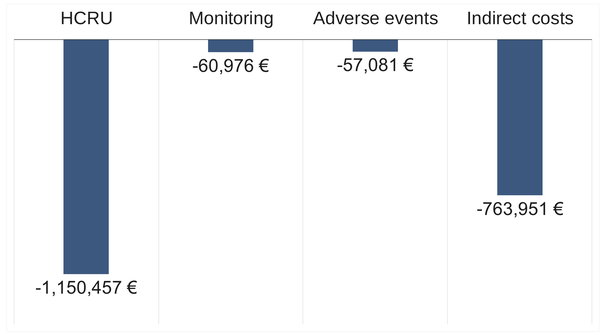


- The introduction of bulevirtide resulted in a reduction of the total expenditure over 10 years from 35 to 33 million euros compared to the actual scenario (**Table 1**). In general, all cost items were reduced with the introduction of bulevirtide (**Figure 3**)

Table 1. Cost of illness in current and new scenario among 1,000 patients

COSTS	Current costs	New scenario
Cost of Illness	**€ 35,117,179**	**€ 33,084,713**
HCRU	€ 12,617,929	€ 11,467,472
Monitoring	€ 2,947,289	€ 2,886,313
Adverse events	€ 166,722	€ 109,641
Indirect costs	€ 19,385,239	€ 18,621,288

Figure 3. Cost consequence of introducing bulevirtide over 10-year time horizon among 1,000 patients

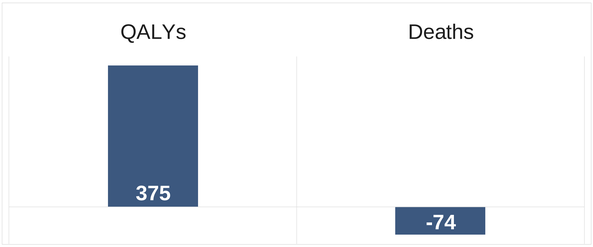


- The introduction of bulevirtide in the new scenario reflected an increase in QALYs from 4,300 to 4,675 and a decrease in the number of deaths from 623 to 548, as shown in **Table 2** below. Impacts are shown in **Figure 4**

Table 2. Impact on outcomes in current and new scenario among 1,000 patients

OUTCOMES	Current scenario	New scenario
QALYs	4,300	4,675
Deaths	623	549

Figure 4. Difference in outcomes between current vs. new scenario among 1,000 patients



Limitations

- Data available for transition probabilities in the natural history of HDV and the disease progression of individuals responding to treatment are not strictly based on Italian patients
- Absence of sufficient data to establish a direct connection between the combined response endpoint and a reduction in HDV progression and clinical events
- Treatment cost was not considered. However, the aim of the study was to analyze the impact on other direct health costs and health outcomes