### Background

- Chronic Hepatitis B (CHB) is caused by chronic infection with Hepatitis B Virus (HBV) and represents a major global health problem. Traditional CHB treatments are lamivudine (LAM) and interferon-α2b (IFN). Peginterferon-α2a (PEG) has been recently approved for the treatment of CHB disease.

- PEG is more effective than LAM or IFN in chronic HBV infection, but also more expensive. Several pharmacoeconomic modelling studies demonstrated cost-effectiveness and cost-utility of PEG in US and other countries. To our knowledge, the economic impacts of these alternatives in Italy, where health care services organization, funding system, and costs structure presents peculiarities, have not been compared yet.

### Objective

- To assess the economic and clinical impact of the use of peginterferon-α2a (40KD) versus LAM for the treatment of HBV-negative CHB disease in Italy.

### Methods

#### Model description

The evaluation has been performed by reviewing and adapting the Italian context of an international model simulating CHB disease.

- CHB disease course is simulated with the use of a Markov model, which simulates the progression of disease in two disease states, namely HBeAg-negative and HBeAg-positive CHB.

- Three base-case scenarios were developed and evaluated:
  - HBeAg-negative, trial-based scenario: HBeAg-negative patients, LAM (100 mg once daily) vs. PEG (150 μg once a week), both for 48 weeks.
  - HBeAg-negative, long-term scenario: HBeAg-negative patients, LAM (100 mg once daily) for 208 weeks (4 yrs) vs. PEG (150 μg once a week) for 48 weeks.
  - HBeAg-positive, trial-based scenario: HBeAg-positive patients, IFN (4.5 MU 3 days a week) vs. PEG (180 μg once a week), both for 24 weeks.

- Conclusively, with data from trials, response is defined as ALT normalization and HBV DNA < 20,000 copies/ml, at the end of follow-up for HBeAg-negative patients and as HBe- seroconversion for HBeAg-positive patients.

Clinical outcomes measured were average years life gained (YLS) and quality-adjusted life years (QALYs).

#### Costs and quality of life

- Costs were evaluated adopting National Health Service perspectives as only direct medical costs were considered.

- Pharmaceutical costs are based on net ex-factory prices as of January 2006. Resulting weekly treatment costs are €186.02 for PEG, €147.77 for LAM, and €174.14 for IFN.

- Other state direct medical costs derive from Italian costs published in a multinational study (Brown, 2004) and include GP and specialist visits, diagnostics, hospitalizations, pharmaceutical treatments different from antiviral therapy.

- State-specific utility weights are extrapolated from the original model, which in turn derived these values from published data (Hong, 1995; Bennet, 1997).

- An annual discount rate of 3.5% is applied to both future costs and health benefits.

#### Sensitivity analysis

- Both probabilistic and deterministic one-way sensitivity analyses were conducted.

- In the deterministic sensitivity analysis, uncertainty ranges considered are ±10% for treatments response rates, ±15% for treatment pharmaceutical costs, ±25% for other state-specific direct medical costs, ±20% for indirect costs, and ±20% for utility weights. Sensitivity on discount rates has been evaluated, being the value of 1.5% on benefits and 6% on costs.

- Probabilistic sensitivity analysis (PSA) is performed through Monte Carlo simulation. Randomization distributions, representing uncertainty of uncertain monetary values, are based on probability distributions, log-normal and normal for costs and effectiveness parameters, respectively. Results of PSA are presented as cost-effectiveness acceptability curves (CEACs).

### Results

#### Base-cases

In every investigated scenario the treatment with PEG results more effective and more expensive than LAM or IFN. Costs increase as the higher price of PEG is only slightly compensated by a reduction in other direct medical costs. Incremental cost-utility ratios are €8,632/QALY, €8,368/QALY and €8,714/QALY in the HBeAg-negative trial-based, HBeAg-negative long-term and HBeAg-positive scenarios respectively.

#### Sensitivity analysis

- In the HBeAg-negative trial-based scenario one-way sensitivity analysis shows that incremental cost-utility ratio for PEG vs. LAM ranges from 3,460 €/QALY estimated by applying different discount rates for benefits (3%) and for costs (6%) to 15,100 €/QALY when relative utility is set to 0.79 (lower extreme of tested range). Similar results were obtained for the HBeAg-negative long term scenario.

- In HBeAg-positive scenario cost-utility of PEG vs. IFN ranges from 5,100 €/QALY when 1% and 8% discount rates for direct costs and benefits are applied, to 17,000 €/QALY when relative utility is set to its lower extreme.

- PSA is implemented through a second order Monte Carlo simulation on a sample of 1,000 iterations. CEAC plot indicates the probability that the treatment tested is actually cost-effective in function of the willingness to pay for an additional unit of cost-effectiveness (€/QALY). For instance, in the HBeAg-negative trial based scenario, the probability that cost-utility of PEG vs. LAM will be lower than 12,000 €/QALY corresponds to 92%. Thus, if a health decision-maker or a community is willing to pay up to 12,000 € to gain one QALY, the choice to treat CHB with PEG instead of LAM will be appropriate in 92% of cases.

- The PSA on HBeAg-negative long term based scenario shows a higher variability and instability of the results of the model. This is mainly due to the small difference between PEG and IFN effectiveness which give a deeper cave to skew in the incremental cost-effectiveness ratio.

### Conclusions

- Our model indicates that PEG is associated with higher benefits at an increased cost with respect to LAM and IFN, with a cost-utility ratio around 8,500 €/QALY in the three investigated scenarios.

- Deterministic sensitivity analysis shows that variation of response ratio utility, PEG response rate and applied discount rates could importantly affect presented results, possibly leading to doubled cost-utility ratios. Nevertheless, PSA shows that if a decision maker is willing to pay up to 12,000 € for an extra QALY, the probability of PEG being cost-effective is comfortably high.

- In general, although literature data are not homogenous, health care strategies with a cost/QALY between 25,000 and 50,000 dollars are usually considered cost-effective. If we adopt these thresholds the acceptability of the treatment is even more evident.

#### References


