OBJECTIVES: To evaluate, in daily practice, the benefits of drotrecogin alfa (DA) in the treatment of severe septic patients with multiple organ failure and optimum intensive care support.

METHODS: In this prospective, observational pre-post study, the clinicians were free to include any patient meeting DAs inclusion criteria before and after DAs marketing. An optimal propensity score matching technique was used to reduce recruitment bias. Survival was modeled using a Cox proportional hazards model with a shared frailty term to account for the clustering of patients within the intensive care units. The number of bleeding events measured DAs safety.

RESULTS: Respectively 509 and 587 patients were included in the before and after groups. There is strong evidence of recruitment bias: patients in the after group are younger, more frequently ventilated, have less comorbidities but more organ failures. After propensity score matching, 340 patients were retained in the analysis, with a better balance between the groups. The use of a frailty model improves significantly the variance explained by the survival model, showing a non-negligible cluster effect. When considering the whole sample of patients, without adjustments, survival is improved in the after (i.e. with DA) group (p = 2.5%), with a hazard ratio (HR) of 0.805. In the matched sample, there are no significant survival differences (HR = 0.900, p = 35.0%). However, after stratifying by the LOS severity score quartiles, significance is reached (HR = 0.795, p = 4.8%). In the matched sample, a negative binomial model best described bleeding events. In this model, patients in the after group have a higher mean of bleeding events (p = 2.0%).

CONCLUSION: This observational study confirms DAs clinical trial results in the real practice setting. However, the use of the propensity score cannot replace randomization to assure perfect balance for all patient characteristics, measured and unmeasured. The results should therefore be considered with caution.

ECONOMIC IMPLICATION OF HEPATITIS B VIRAL (HBV) LOAD REDUCTION FOR ENTECAVIR IN HEPATITIS B E ANTIGEN-POSITIVE CHRONIC HEPATITIS B (CHB) PATIENTS

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OBJECTIVES: To evaluate the cost effectiveness of entecavir in reducing HBV DNA viral load (VL) and subsequent compensated cirrhosis (CC), decompensate cirrhosis (DC), and hepatocellular cancer (HCC).

METHODS: The analytic perspective was that of a third-party payer. We used patient-level drug exposure and VL data from a randomized phase III trial of 715 HBeAg+ CHB patients, and estimates of cost offsets and life expectancy gains as a result of the prevention of projected clinical events. The multivariate-adjusted relative risks with VL categories were estimated by Cox proportional hazards models from a Taiwan cohort of 3851 CHB subjects with 42,115 person-years of follow-up, and then applied to the trial patients whose VL were measured at Week 48 to estimate event risks. Entecavir and lamivudine were assigned daily prices of $19.43 and $6.14 respectively, based on recent First Data-Bank reports. Life expectancy for DC and HCC was estimated by the declining exponential approximation of life expectancy (DEALE) method. Other model parameter values were derived from external sources. The uncertainty surrounding event distribution and treatment failure rates beyond trial period were considered using probabilistic sensitivity analyses (PSA) with 1000 replicates.

RESULTS: Subjects were male (75%), Asian (57%) or white (40%) with mean age 35 years. Entecavir was superior to lamivudine for the proportion of subjects who achieved HBV DNA < 300 copies/ml by PCR, assay at Week 48 (67% versus 37%, respectively) (p < 0.05). One year of entecavir therapy gained 0.7843 quality-adjusted life year (QALY) at an incremental cost of $1607, with a 3% annual discount. Compared with lamivudine, using entecavir cost an incremental $2049 per QALY gained (95% CI: $688, $5134), with 98.8% of PSA-derived estimates below $10,000/QALY. Results are robust and most sensitive to treatment duration, efficacy, and cost.

CONCLUSIONS: Entecavir given for one year is clinically effective and highly cost-effective in HBeAg+ patients.

COST-EFFECTIVENESS ANALYSIS OF COMBINED THERAPY WITH PEGINTERFERON ALFA 2A (40 KD) (PEGASYS®) AND RIBAVIRIN (COPEGUS®) IN PATIENTS WITH CHRONIC C HEPATITIS (CHC) AND PERSISTENTLY NORMAL ALT LEVELS (PNALT)

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OBJECTIVE: To establish the clinical prognosis, costs and cost-effectiveness of peginterferon alfa-2a (180 mcg/week) plus ribavirin versus no treatment in patients with CHC and PNALT from a Spanish national health care system (NHS) perspective.

METHODS: A Markov model was developed to simulate the disease progression of 45-year old patients with CHC and PNALT. Fibrosis progression rates in PNALT were obtained from published studies. Efficacy, in terms of sustained virological response (SVR), for peginterferon alfa-2a plus ribavirin and no treatment in patients with genotype 1 and genotype 2/3 was obtained from a multinational, randomized, controlled trial. In this trial, no patients in the control arm achieved an SVR. Transition probabilities and quality of life estimates were obtained from published literature. Unit costs were obtained from a Spanish database. The discount rate employed was 3.5%.

RESULTS: In genotype 1 patients, peginterferon alfa-2a plus ribavirin compared with no treatment increases patients life expectancy by 0.63 years (0.70 quality-adjusted life years (QALYs)), yielding an incremental cost-effectiveness ratio (ICER) of 14,729/€ (93,388/QALY). In genotype 2/3 patients, peginterferon alfa-2a plus ribavirin increases life expectancy by 1.14 years (1.26 QALYs), yielding an ICER of 109/€/LYG (99/€/QALY). The overall ICER based on the genotype distribution in the trial is €11,374/LYG (€99,952/QALY). CONCLUSIONS: From the Spanish NHS perspective, peginterferon alfa-2a (40 KD) (PEGASYS®) plus ribavirin (COPEGUS®) in patients with CHC and PNALT is a cost-effective treatment option, regardless of HCV genotype.

COST-EFFECTIVENESS ANALYSIS OF ALTERNATIVE ANTIMICROBIAL TREATMENTS FOR COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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OBJECTIVE: To evaluate the cost-effectiveness of the empirical use of moxifloxacin in community-acquired pneumonia (CAP) taking into account clinical failure caused by prevailing levels of antimicrobial resistance in France, Germany and the US representing high, low and moderate levels of resistance respectively.

METHODS: Only anecdotal evidence is available in the literature on the direct link between resistance and clinical failure. A