A Patient-Level Simulation Model for Economic Evaluation of Cinacalcet in the Treatment of Secondary Hyperparathyroidism (SHPT) in Italy

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INTRODUCTION

- A large number of patients with chronic kidney disease (CKD) are affected by secondary hyperparathyroidism (SHPT) characterized by elevated secretion of parathyroid hormone (PTH). SHPT leads to disorders of calcium (Ca) and phosphorus (P) metabolism and is associated with an increased risk of cardiovascular calcifications, arterial dysfunction, fracture and morbidity and mortality. Guidelines for managing SHPT, established by the National Kidney Foundation – Kidney Disease Outcomes Quality Initiative (NKF – KDOQI), recommend optimal ranges for Ca, P, PTH serum levels [1].

- Cinacalcet, the first and currently, calcimimetic agent approved for clinical use, allows obtaining an effective long term reduction in serum PTH levels and a better achievement of NKF – KDOQI guideline targets when added to the standard treatment [2][3][4].

OBJECTIVE

- We developed a simulation model to assess the pharmacoeconomic performance, from the perspective of the Italian National Health Service (INHS), of cinacalcet when added to standard treatment (ST) with respect to ST alone.

METHODS

- A patient-level probabilistic Markov model has been developed with TreeAge Pro 2009 (TreeAge Software Inc., Williamstown, MA).

- Each simulated patient is defined with his/her unique characteristics of gender, age and levels of serum Ca, P and PTH. The simulation spans over the whole patient’s lifetime in 8-weeks cycles. An annual discount rate of 3.5% is applied to costs and benefits. Three states are considered: “SHPT”, “SHPT-PxT”, occurring when a patient undergoes parathyroidectomy surgery (PTx), and the “Dead” state. During the simulation, the occurrence of fractures and cardiovascular (CV) events is recorded and these events can impair quality of life (QoL) and generate hospitalization costs.

- The model simulates the effect of cinacalcet (Mimpara®) on Ca, P, and PTH levels of individual patients depending on their initial values.

METHODS (continued)

- The simulation of the trend in time is based on the data from the OPTIMA study [4], a recent European multicenter, open-label, 23-weeks study. The model then correlates the Ca, P and PTH levels with mortality and morbidity on the basis of published evidences.

- The probability of death at each time is calculated as a function of sex, age and the concentrations of PTH, Ca and P. The function is based on the Italian general population mortality [5], factored by a relative risk (RR) to account for the dialysis [6], further multiplied by RR factors accounting for the levels of PTH, Ca and P [7][8].

- The probability of CV events, fractures and PTx is also conditioned on PTH, Ca and P levels [7][9][10][11][12]. PTH affects subsequent mortality, as reported by a large study [13]. PTx also influences the risk of subsequent fracture [11].

- Utilities derive from a prospective cross sectional survey of 180 end-stage renal failure patients with and without co-morbidities.

- Considered costs are related to: cinacalcet and ST (vitamin D sterols and phosphate binders) purchasing, dialysis, CV events and fractures management, and PTx procedures.

- The effectiveness is measured in terms of life expectancy (LE), quality-adjusted life expectancy (QALE) and time in which the levels are controlled, i.e. below the upper limit recommended by the KDOQI guidelines (TiR – time in range).

RESULTS

- Results are calculated with 10,000 iterations. The patient-level, probabilistic simulation allows to take into account for both the inter-individual variability due to patient characteristics and the uncertainty on model parameters, providing the probabilistic sensitivity analysis incorporated with the main results.

- Cinacalcet-treated patients had a mean (SD) increase in TiR of 5.60 (6.57), 3.45 (6.85), 1.62 (5.64) and 2.85 (5.60) discounted patient years for PTH, Ca, P and all parameters, respectively. Mean LE extension was 1.16 (3.74) life-years and QALE increase 0.77 (2.63).

CONCLUSIONS

- The model can represent an advancement with respect to the existing two [14] as:
  - It keeps into account all the three PTH, Ca and P parameters and simulates a quasi-continuous trend with time for individual patients;
  - Deaths, CV events, fractures and PTx derive from PTH, Ca and P imbalances, as indicated by recent correlation publications.

REFERENCES


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