LANTHANUM CARBONATE FOR HYPERPHOSPHATEMIA IN CHRONIC KIDNEY DISEASE BEFORE AND DURING DIALYSIS: A COST-EFFECTIVENESS ANALYSIS IN SPAIN

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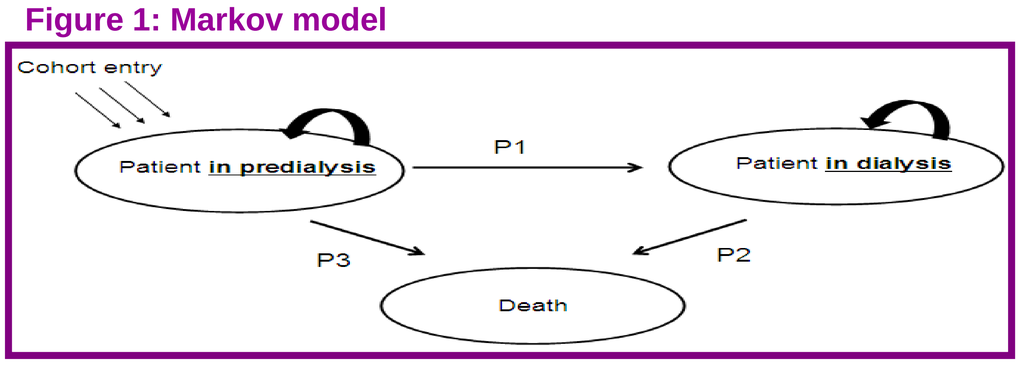
BACKGROUND

•Calcium-based (CB) phosphate binders are recommended as first-line treatment of hyperphosphatemia in Chronic Kidney Disease (CKD).
•However, when calcium agents are ineffective or inadequate, a strategy of dose escalation may be inappropriate due to the increased risk of hypercalcemia[1], related to a higher mortality risk[2].
•The aim of this study was to evaluate the cost-effectiveness of the use of Lanthanum Carbonate (LC) as second line treatment in CKD patients irrespective of dialysis status, in Spain.

METHODS

•Markov model was developed considering three health states (predialysis, dialysis and death) to assess the incremental cost-effectiveness ratio (ICER) of second-line LC treatment in patients, previously treated with CB (calcium carbonate and calcium acetate). (Figure 1)
•This analysis was conducted on an hypothetical cohort of 1,000 patients who are initially not on dialysis, from the Spanish healthcare service perspective, considering a life-time horizon.
•CKD progression (P1) was obtained from randomized clinical trials[3,4,5] and from the European Dialysis and Transplant Association annual report[6], adjusted with the relative risk related to serum phosphorus (SP) levels[7].
•General survival was extracted from the European Renal Association-European Dialysis and Transplant Association Annual Report6 and adjusted with the relative risk related to SP levels in predialysis (P2)[8] and dialyzed patients (P3)[9].

Figure 1: Markov model



•Patients started treatment when SP level exceeded 4.6mg/dl10 for predialysis and 5.5 mg/dL for dialyzed cohort[11]. The model considered a SP target level of 4.6 mg/dL[3] for both populations.
•Efficacy data for CB and LC in dialyzed patients were based on a Phase III, randomized, active comparator-controlled trial[4].
•Due to low number of predialysis patients treated with LC, treatment efficacy in this cohort was based on pooled patient level data of predialysis and dialyzed populations with similar baseline clinical characteristics (SP baseline values, age and glomerular filtration rate)[3,5].
•One-way and probabilistic sensitivity analysis (10,000 Montecarlo simulations) were performed to test the robustness of the model and to determine the impact of uncertainty on the incremental cost-effectiveness ratio.

Costs and Utilities

•In accordance with perspective, only direct costs (pharmaceutical and dialysis costs) were included.
•Drug costs were derived from ex-factory prices12, adjusted with 7.5% mandatory rebate[13,14].
•Dialysis costs (2013 prices in Euros) were obtained from diagnosis-related groups[15]. Dialysis costs in added life years were classified as unrelated future costs and were not considered in the base case analysis.
•Utilities for predialysis (0,71) and dialysis (0,61) were based on literature[16].
•The incidence of vomiting was estimated to be 4.0% for predialysis[3], and 7.2% in dialysis patients4 based on published data. An utility decrement of 0.0408 was considered for each episode[17].
•Unitary costs are collected in Table 1 and were both discounted at 3%[18].

Pharmaceutical costs		Presentation cost (ex-factory price[12] including rebate[13,14])	Cost per gram (€/g)	Annual treatment cost *Predialysis*	Annual treatment cost *Dialysis*
Lanthanum carbonate					
Fosrenol® 750 mg	90 chewable tablets	€167.86	€2.48	€1,702	€2,042
Calcium binders (average CC, CA)				€49	€93
Calcium carbonate					
Mastical® 1,250 mg	60 chewable tablets	€2.09	€0.027	€30	€50
	90 chewable tablets	€2.97			
Calcium acetate					
Royen® 1,250 mg	60 chewable tablets	€7.13	€0.124	€68	€136
	120 chewable tablets	€3.91			
Dialysis costs[13]					€42,556

RESULTS

•Considering a lifelong time horizon, costs per patient associated with LC second line therapy were €1,169, while they were €5,044 with the CB only strategy. **(Table 2)**
•Second line LC delayed progression to the dialysis health-state, thereby leading to large cost-savings. On average, patients accrued 4.579 Quality Adjusted Life Years (QALYs) in the LC second line treatment strategy, compared to 4.653 QALYs in the CB only strategy.
•LC therapy was a dominant strategy (i.e. lower costs, higher QALYs) over continuous CB treatment.
•One-way sensitivity analyses revealed that time horizon and the inclusion of unrelated future costs were the most influential parameters in the model. **(Table 3)**
•Assuming a €30,000/QALY threshold19, LC was cost-effective as second line treatment in 100% of PSA simulations. **(Figure 2)**

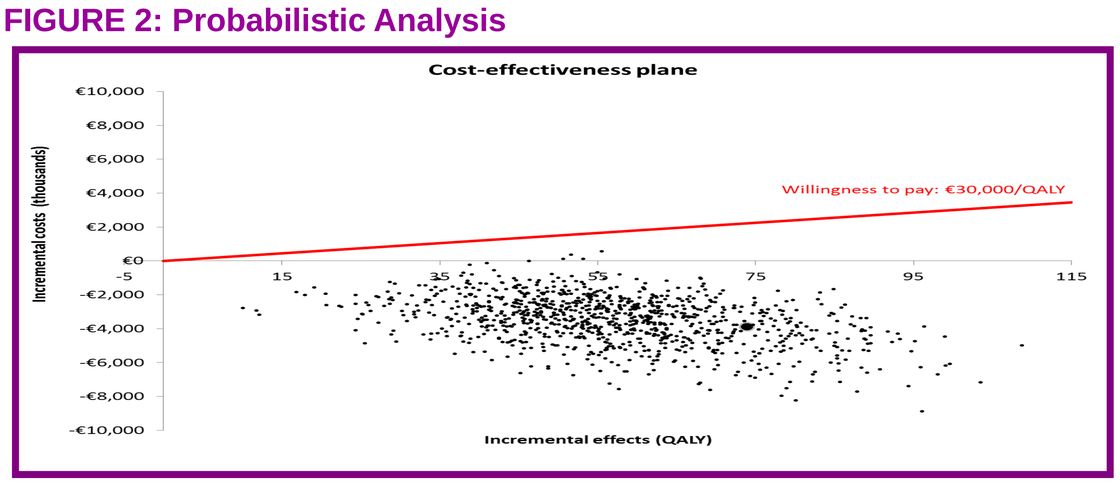
TABLE 2: Base Case Results

FULL COHORT	Continuous CB	Second line LC	Incremental (LC vs CB)
Therapy response			
Number of responders in predialysis	445	658	213
Number of responders in dialysis	-60	-57	3
Total number of responders	385	601	216
Health outcomes			
Life Years	6,868	6,981	113
Dialysis free years	0	108	108
QALY	4,579	4,653	74
Costs –(€, 2013)			
Total costs (€ thousand)	€5,044	€1,169	- €3,875
Drug costs (€ thousand)	€468	€1,169	€ 701
Dialysis costs (€ thousand)	€4,576	€0	
Cost-effectiveness incremental ratio (ICER)			
Cost per life-year gained (€)			Dominant
Cost per QALY gained (€)			Dominant
Net monetary benefit (€ thousand)			€6,092

TABLE 3: One-way Deterministic Analysis

	Incremental costs CL vs CB	Incremental QALY CL vs CB	ICER (€/QALY)	% Variation vs Base Case
BASE CASE	**€ 3,875.1**	**74**	**- €54,449**	
Time horizon (5 years)	- € 1,616.3	26	- €63,381	20.8%
Time horizon (10 years)	- € 2,891.7	49	- €59,416	13.3%
Included unrelated future dialysis costs	- € 3,365.9	74	- €45,557	-13.1%
Dialysis target level 5 mg/dL	- €3,661	79	- €46,166	-12.0%
Annual Discount Rate (6%)	- € 4,998.5	99	- €50,248	- 4.2%
Annual Discount Rate (0%)	- € 3,085.7	57	- €54,187	3.3%
Only considering Acetate carbonate	- € 3,582	70	- €51,504	-1,8%
Only considering Calcium carbonate	- € 4,197.9	79	- €53,121	1.3%

FIGURE 2: Probabilistic Analysis



CONCLUSIONS

• LC has demonstrated to be an efficient strategy, considered a dominant option, as second line treatment of hyperphosphatemia in CKD patients irrespective of dialysis status

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