COST-EFFECTIVENESS ANALYSIS OF DIFELIKEFALIN FOR THE TREATMENT OF MODERATE TO SEVERE PRURITUS ASSOCIATED WITH CHRONIC KIDNEY DISEASE (CKD-aP) IN SPAIN

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INTRODUCTION

- Chronic kidney disease-associated pruritus (CKD-aP) is a disabling condition affecting around 60% of patients on haemodialysis in Spain[1].

OBJECTIVES

- This study aimed to assess the cost-effectiveness of difelikefalin versus the best supportive care (BSC) for the treatment of moderate to very severe CKD-aP in adult patients under haemodialysis, from the perspective of the Spanish National Healthcare Service. Difelikefalin is the only drug approved in Europe for the treatment of CKD-aP in haemodialysis patients[2].

METHODS

- A Markov model was developed with the following seven health states: no CKD-aP; mild; moderate; severe; and very severe CKD-aP; renal transplant; and death. The model included patients with baseline moderate to very severe CKD-aP, consistent with difelikefalin clinical phase III trials (KALM-1 and -2) and its SmPC[2,3]. Transition probabilities were calculated based on patient movement between pruritus health states over time, using the 5-D itch scale as the efficacy endpoint and based on difelikefalin phase III trials results (Table 1)[3,4].
- The model included costs related to hospitalization due to septic shock and bacteraemia, adverse events, and pharmacological treatment (Table 2).
- Costs and quality-adjusted life years (QALYs) were discounted at 3% annually over a 36-year lifetime horizon.

Table 1. Difelikefalin Phase III Trials results.

Phase III Trials Results[3,4]									
Study	**KALM-1**			**KALM-2**			**Pooled data**		
Group	Placebo n=188	DFK n=189	P value	Placebo n=236	DFK n=237	P value	Placebo n=425	DFK n=426	P value
Δ from baseline to week 12 in total 5-D itch score (95% Confidence Interval)	-3.7 (-4.4,-3.1)	-5.0 (-5.7,-4.4)	< 0.001	-3.8 (-4.5,-3.1)	-4.9 (-5.6,-4.2)	0.002	-3.7 (-4.1,-3.3)	-4.9 (-5.4,-4.5)	< 0.001

Table 2. Cost and percentage of use of pharmacological treatments.

Treatment	Moderate CKD-aP[5,6]	Severe CKD-aP[5,6]	Very severe CKD-aP[5,6]	Cost per 28-day cycle[7]
Difelikefalin				**270.63€**
Topic immunosuppressant	1.60%	7.40%	7.40%	**1.40 €**
Oral corticosteroids	8.10%	16.00%	16.00%	**1.49 €**
Antihistamines	13.80%	24.70%	24.70%	**3.81 €**
Pregabalin / Gabapentin	6.50%	17.30%	17.30%	**3.27 €**
Montelukast	0.80%	1.20%	1.20%	**13.49 €**
Antidepressants	17.90%	21.00%	21.00%	**8.49 €**
Anxiolytics	1.60%	4.90%	4.90%	**1.79 €**
Medication to improve quality of sleep	51.00%	72.00%	72.00%	**3.73 €**

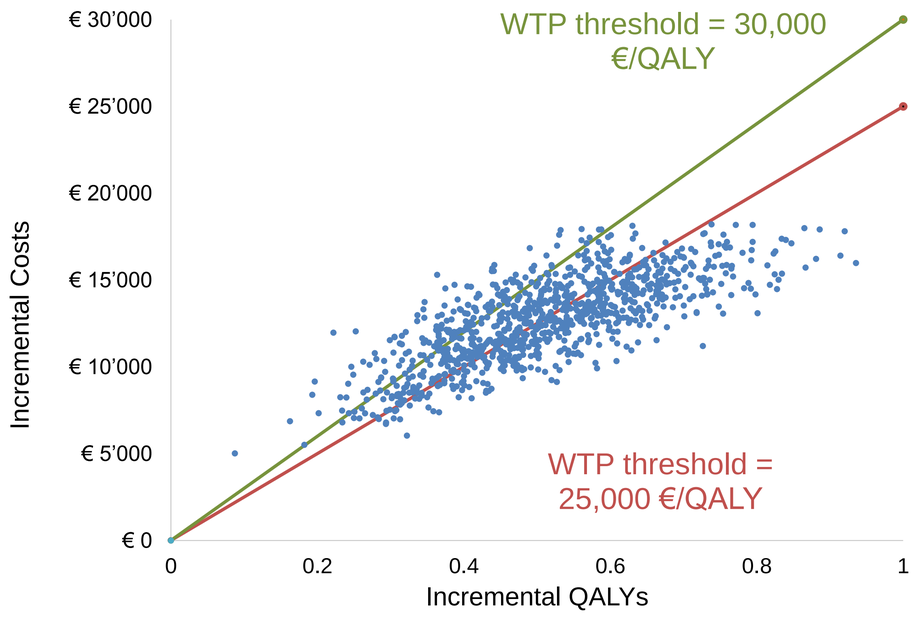
RESULTS

- Difelikefalin treatment was associated with an average increased of efficacy per patient of 0.49 QALYs and higher average costs per patient (+12,300€) compared to the BSC. Using a placeholder cost of 270.63€ per 28-days for difelikefalin, the incremental cost-utility ratio (ICUR) was 25,000€/QALY (Table 3).
- The resulting ICUR suggests that difelikefalin could be a cost-effective treatment option considering the 25,000-30,000 €/QALY willingness-to-pay threshold (WTP,) which is accepted in Spain for economic evaluation studies[8].
- The deterministic sensitivity analysis (DSA) confirmed the robustness of the results, with mild and moderate CKD-aP utility values and difelikefalin cost as the main drivers.
- The probabilistic sensitivity analysis (PSA), undertaken using 1,000 iterations, yields 48% and 84% probabilities of difelikefalin being cost effective at the 25,000 €/QALY and 30,000 €/QALY WTP thresholds, respectively[8] (Figure 1).
- In 100% of the simulations, the ICUR was found to be in the north-east quadrant of the plane, meaning difelikefalin was always more effective and associated with higher costs than the BSC.
- Regarding the evolution of the disease estimated via transition probabilities, patients treated with difelikefalin were more likely to end up in the mild or no CKD-aP health states when compared to BSC treated patients.

Table 3. Base Case Cost-Effectiveness Discounted Results.

Discounted base case results	Difelikefalin	BSC	Difference
Costs	21,741 €	9,441 €	12,300 €
QALYs	2.81	2.32	0.49
ICUR	**25,000 €/QALY**		

Figure 1. Incremental Cost-Effectiveness Plane.



CONCLUSIONS

- Difelikefalin could be a cost-effective option compared to the BSC for the management of CKD-aP in adult patients under haemodialysis in Spain. Considering the unmet medical need, these results reinforce the economic benefits of in label treatment with difelikefalin in routine clinical practice in Spain.

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DISCLOSURES. **This study was sponsored by Vifor Fresenius Medical Care Pharma España.**

Poster presented at ISPOR Europe 2024, 17th-20th November 2024, Barcelona, Spain