(5). CKD-associated Pruritus (CKD-aP), commonly referred to as uremic pruritus, is a serious, systemic itch comorbidity that occurs in CKD patients, particularly those undergoing dialysis, and is common among kidney failure patients (6). It is associated with poor quality of life (QoL), sleep disturbance, anxiety, and depression, as well as increased risks of infection, hospitalisation, and mortality (6, 7).

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Cost-effectiveness of difelikefalin for the treatment of moderate to severe chronic kidney disease-associated pruritus (CKD-aP) in adult patients receiving in-centre haemodialysis

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C. Collins[1], T. Edmonds[1], I. Taylor[1], O. Darlington[1], A. Mumford[1], T. Schaufler[2], M. Soro[2], G Baxter[3]

1. Initiate Consultancy, London, UK; 2. CSL Vifor, Glattbrugg, CH; 3. CSL Vifor, Staines-upon-Thames, UK

Study sponsored by CSL Vifor

SUMMARY

OBJECTIVES

- CKD-aP is linked to poor HRQoL, as well as increased risks of adverse health outcomes.
- Difelikefalin has shown to be effective in treating moderate to severe CKD-aP in two Phase 3 trials.
- This study assessed the cost-effectiveness of difelikefalin and BSC versus BSC alone for adults with moderate to severe CKD-aP receiving in-centre haemodialysis within the NHS in the UK.

METHODS

- A Markov model was constructed categorising pruritus severity into five different health states. Renal transplant and death were defined as absorbing states.
- An initial 12-week period was modelled to assess patients' initial treatment response, followed by a long-term effectiveness period to reflect the costs and benefits of difelikefalin and BSC over a patient's lifetime.

FINDINGS

- Treatment with difelikefalin and BSC was associated with increased life expectancy and increased quality adjusted life years compared with BSC alone, at an incremental cost of £7,814 per person.
- At £31.90/vial, difelikefalin was cost-effective at a WTP threshold of £30,000/QALY.

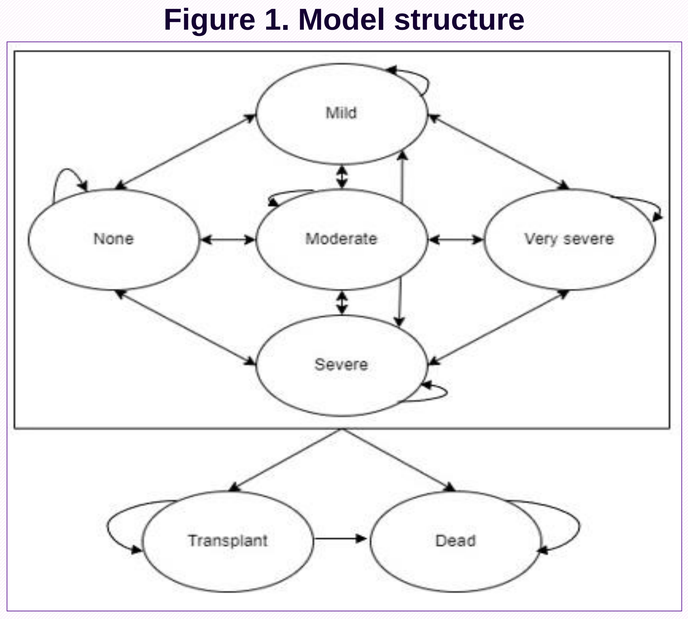
BACKGROUND & AIMS

- Chronic Kidney Disease-associated Pruritus (CKD-aP), formerly referred to as uremic pruritus, is a serious, systemic itch comorbidity which occurs in CKD patients, particularly those undergoing dialysis, and is common among kidney failure patients (1). It is associated with poor health-related quality of life (HRQoL), sleep disturbance, anxiety, and depression, as well as increased risks of infection, hospitalisation, and mortality (1,2).
- With the exception of difelikefalin (DFK), there are currently no licensed medicines specifically for CKD-aP.
- Difelikefalin has been demonstrated to be an efficacious treatment for moderate to severe CKD-aP in two placebo-controlled Phase 3 trials: KALM-1 and KALM-2 (1,2).
- The objective of this study was to estimate the cost-effectiveness of difelikefalin in addition to best supportive care (BSC) for the treatment of adults with moderate to severe CKD-aP undergoing in-centre haemodialysis from a UK payer perspective.

METHODS

- A lifetime Markov model, comprising five health states defined by pruritus severity, was constructed to estimate costs and outcomes for CKD-aP patients treated with difelikefalin in combination with BSC, compared with BSC alone (Figure 1).

Figure 1. Model structure



- Please see Table 1 for details on how different parameters were modelled.
- The 5-dimension (5-D) Itch scale is a multidimensional questionnaire which assesses itch severity and itch-related quality of life over the previous 2 weeks.
- Treatment-specific transition probabilities between CKD-aP severity categories were derived from the pooled trial data. The total 5-D Itch scale score was used to model patients change in itch severity.
- The model comprises an initial 'run-in' period to reflect short-term treatment decisions and initial response to treatment, whereby patients on difelikefalin who do not achieve a clinically significant response (improvement in 5-D Itch scale score ≥ 5) will discontinue treatment.
- Transition matrices were derived from per-cycle probabilities of losing or gaining health states. Each cycle has unique transition probabilities: the response to treatment is greatest following initiation of treatment, and overall response is further stratified by baseline CKD-aP severity.

RESULTS

- Treatment with difelikefalin and BSC was associated with increased life expectancy (0.11 years per person) and increased quality adjusted life years (QALYs, 0.26 per person) compared with BSC alone, at an incremental cost of £7,814 per person (Table 2).

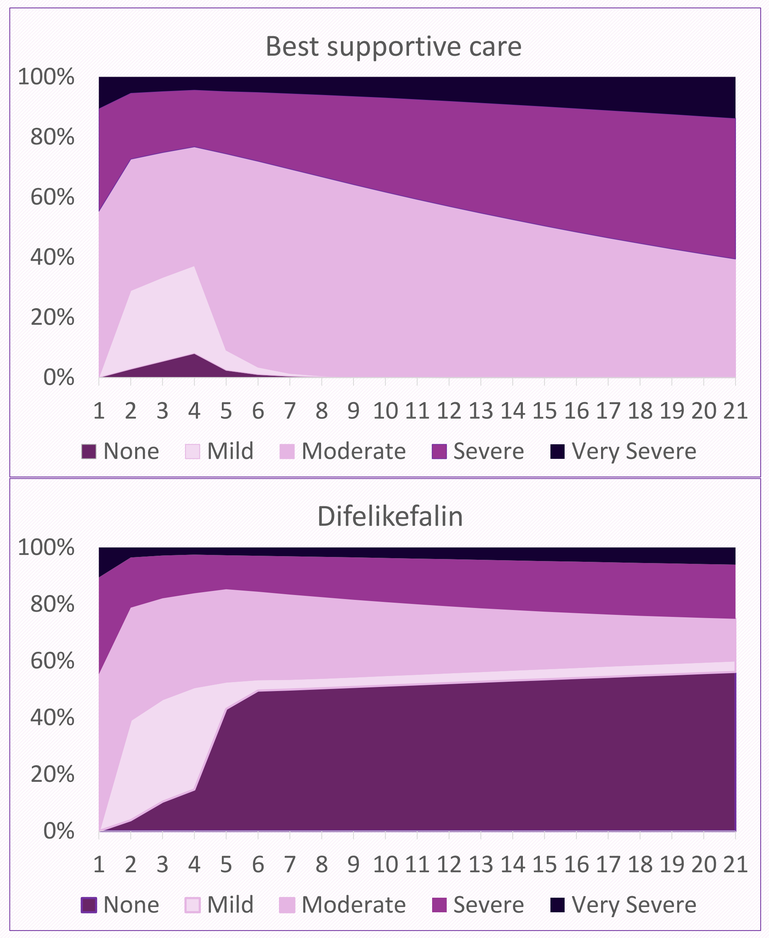
Table 2. Cost-effectiveness results of DFK vs BSC over 42 years.

	DFK	BSC	Incremental
Costs	£31,516	£23,702	£7,814
Life Years	4.64	4.53	0.11
QALYs	3.20	2.93	0.26

- The incremental QALYs were driven by an increase in the number of people in less severe CKD-aP states. The Markov traces in Figure 2 display the distribution of patients across health states for difelikefalin and BSC.
- Benefits were driven by reductions in pruritus severity and consequently improved HRQoL and reduced mortality risk, along with reductions in healthcare resource use and concomitant medications.

- **Difelikefalin was estimated to be cost-effective at a willingness-to-pay threshold of £30,000/QALY and a cost of £31.90/vial.**

Figure 2. Markov traces



- Probabilistic Sensitivity Analysis (PSAs) were performed to explore the effect of uncertainty associated with model inputs (Figure 3)
- The probability of cost-effectiveness is 48% at a willingness-to-pay (WTP) threshold of £30,000/QALY.

Figure 3. Probabilistic Sensitivity Analysis (PSA)

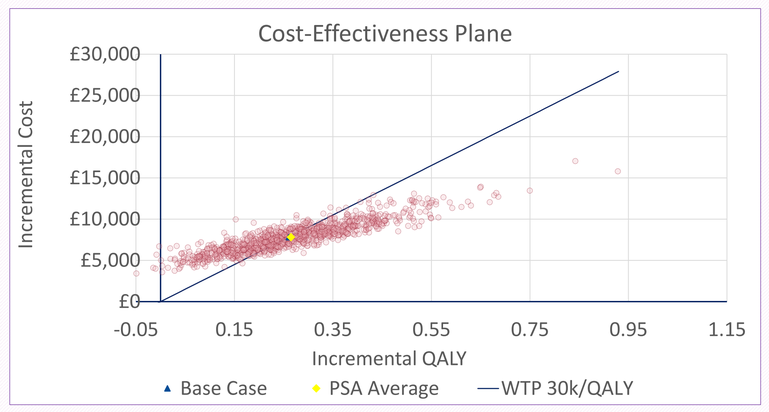


Table 1. Model parameters.

Parameter	How it was modelled and sourced
CKD-aP progression	Based on 5-D Itch scale severity measurements from the KALM trials (1,2)
Mortality and transplantation rates	Using time-dependent probabilities from the UK Renal Registry (UKRR) (3)
Relative risk of hospitalisation and mortality	Applied based on itch severity, informed by the Dialysis Outcomes and Practice Patterns Study (DOPPS) (4)
Utility estimates and costs	Sourced from literature and the National Health Service (NHS) cost collection, and discounted at 3.5% annually (5,6)

Health states	Utility score
None	0.744
Mild	0.726
Moderate	0.589
Severe	0.595
Very severe	0.595
Transplant	0.712

CONCLUSION

- **Difelikefalin plus BSC is a cost-effective treatment for CKD-aP compared with BSC alone, with the potential to ameliorate the significant burden CKD-aP imposes on patients in the UK.**

References

1. *Fishbane S, Wen W, Munera C, Lin R, Bagal S, McCafferty K, et al. Safety and Tolerability of Difelikefalin for the Treatment of Moderate-to-Severe Pruritus in Hemodialysis Patients: Pooled Analysis From the Phase 3 Clinical Trial Program. Kidney Medicine. 2022.*
2. *Topf J, Wooldridge T, McCafferty K, Schomig M, Csiky B, Zwiech R, et al. Efficacy of Difelikefalin for the Treatment of Moderate to Severe Pruritus in Hemodialysis Patients: Pooled Analysis of KALM-1 and KALM-2 Phase 3 Studies. Kidney medicine. 2022;4(8):100512.*
3. *Association UK. UK Renal Registry 25th Annual Report. 2021.*
4. *Sukul N, Karaboyas A, Csomor PA, Schaufler T, Wen W, Menzaghi F, et al. Self-reported Pruritus and Clinical, Dialysis-Related, and Patient-Reported Outcomes in Hemodialysis Patients. Kidney Med. 2021;3(1):42-53 e1.*
5. *Soro M, Thokala P, Fotheringham J POSC312 A Methodological Approach to Assess the Economic Value of Difelikefalin to Treat Chronic Kidney Disease Associated Pruritus (CKD-AP), Value in Health, 2022; 25.*
6. *NHS. National Cost Collection for the NHS. 2022.*

Presented at ISPOR Europe, 12th-15th November 2023

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