Cost-effectiveness of empagliflozin in the treatment of patients with chronic kidney disease in France

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Objectives

The efficacy and safety of empagliflozin in the treatment of chronic kidney disease (CKD) were demonstrated in the EMPA-KIDNEY[1] trial which showed a 28% reduction in combined risks of kidney disease or death from cardiovascular causes (Hazard Ratio: 0.72; 95% confidence interval: 0.64-0.82, p<0.001) compared with placebo. The present study aimed to assess the cost-effectiveness in cost per QALY ratio (quality adjusted life-year) of empagliflozin + standard of care (SoC) compared to SoC alone in the treatment of CKD in France.

Introduction

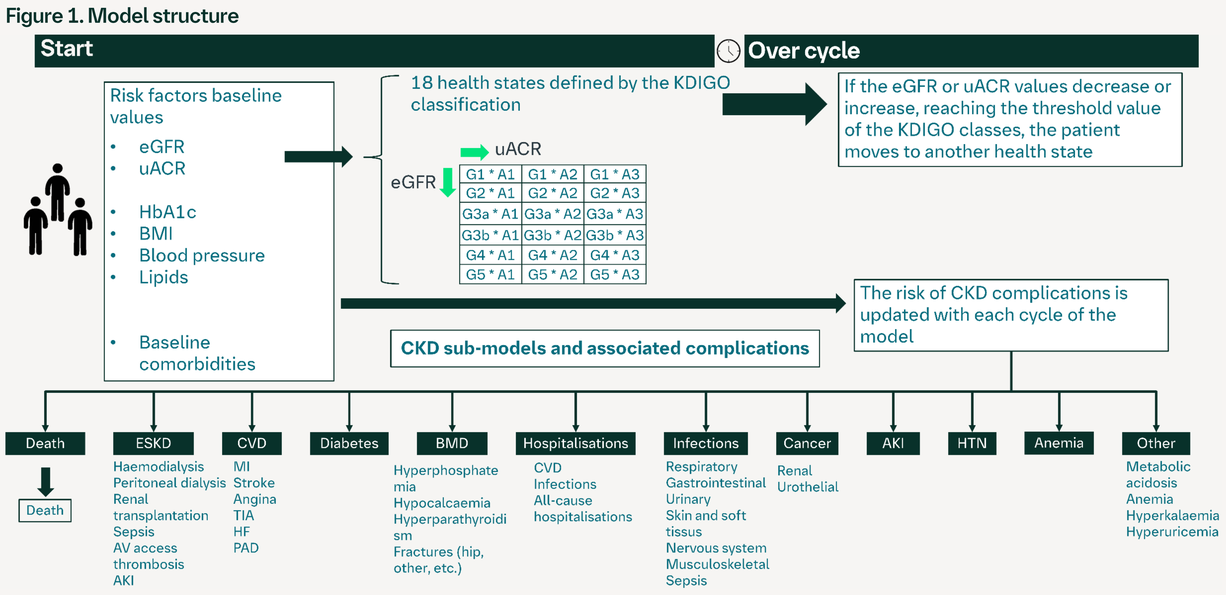
- Chronic kidney disease (CKD) is a condition characterized by a gradual decline in kidney function, marked by a reduced estimated glomerular filtration rate (eGFR) and/or elevated urinary albumin-to-creatinine ratio (uACR) for over 3 months. An early diagnosis is crucial to prevent kidney failure (KF)[1].
- Medical treatment involves preventing CKD progression through blood pressure control, renin-angiotensin system blockade, dietary and glycaemic management, and cardiovascular complication prevention. Empagliflozin, an SGLT2 inhibitor, is used for treating type 2 diabetes and heart failure, and was recently approved for CKD based on EMPA-KIDNEY trial results[2].
- The EMPA-KIDNEY trial found that empagliflozin reduced the risk of CKD progression or cardiovascular death compared to placebo in CKD patients at risk[2].

Methods

Economic model

- A Markov microsimulation model with 18 health states defined with KDIGO classification[1] was developed in patients with CKD treated with empagliflozin in addition to SoC versus SoC alone (Figure 1). Costs and benefits were calculated over a 25-year time horizon with annual cycles.

Figure 1. Model structure



Clinical data

- eGFR and uACR progression were derived from EMPA-KIDNEY clinical trial as per the KDIGO classification[1] (Table 1).
- The risk of complications was based on the initial baseline characteristics and clinical risk factors of the patients. The probability of patients experiencing any complications or events per cycle was predicted by using clinical data from literature (using transition probabilities or incidence rates) or commonly recognised predictive risk equations[3].
- KF was reached at an eGFR < 15 ml/min/1.73m² according to KDIGO classification[1]. Once in KF, patients needed to initiate kidney replacement therapy either with dialysis or a kidney transplant, but they could also receive conservative therapy.

Table 1. KDIGO classification

eGFR categories (ml/min/1.73 m²)	Persistent albuminuria categories range		
	< 30 mg/g	30-300 mg/g	> 300 mg/g
≥ 90	G1*A1	G1*A2	G1*A3
60-89	G2*A1	G2*A2	G2*A3
45-59	G3a*A1	G3a*A2	G3a*A3
30-44	G3b*A1	G3b*A2	G3b*A3
15-29	G4*A1	G4*A2	G4*A3
< 15	G5*A1	G5*A2	G5*A3

Cost and utility parameters

- Both economic and health outcomes were discounted at a 2.5% annual rate in accordance with French guidelines for economic evaluation[4].
- The model included costs related to drugs (empagliflozin and SoC therapies), disease management, event management and KF events. Costs were valued in €2023 and from a healthcare system perspective.

Base case

- Health states utility scores in EQ-5D used in the model are issued from Jesky et al., a prospective observational study on UK population (Table 2)[5]. Once patients reached kidney failure, specific health state utility scores were applied based on the type of renal replacement therapy used (Table 3).
- Health state utility scores from Jesky et al.[5] are assumed to already account for any complications that may arise in patients. Therefore, disutility associated with complications were excluded from the base case analysis of this study to prevent double counting.

Sensitivity analysis 1

- A method for adjustment using a correlation factor based on population utility norms, calculated from the French and UK standards as reported in Szende et al., and weighted by both populations' characteristics, was also explored in a sensitivity analysis (Table 2)[6]. The objective of this sensitivity analysis was to evaluate the potential impact of differences in quality-of-life perceptions between UK and French patients.

Sensitivity analysis 2

- A disutility score from the literature was applied to each complication or event to explore the burden of comorbidities and complications of CKD in a sensitivity analysis (Table 4).

Table 2. Utility scores per CKD health states used in the cost-effectiveness model

Health states	Base case	Sensitivity analysis 1
G1*A1 to G2*A3	0.85	0.88
G3a*A1 to G3b*A3	0.80	0.83
G4*A1 to G4*A3	0.74	0.77
G5*A1 to G5*A3	0.73	0.76

Table 3. Kidney failure specific health states utility scores

Health states	Score	Source
Peritoneal dialysis	0.580	Liem et al.[7]
Haemodialysis	0.560	
Kidney transplant (1st year)	0.710	TA775-Dapagliflozin for treating chronic kidney disease[8]

Table 4. Disutility scores per complication/event used in the cost-effectiveness model in sensitivity analysis 2

Complication/event	Disutility score	Source
Cardiovascular comorbidities and complications – per event		
Myocardial infarction	-0.055	Beaudet et al.[9]
Unstable angina	-0.090	
Stroke	-0.164	
Congestive heart failure	-0.108	
Transient ischemic attack	-0.070	
Peripheral artery disease	-0.061	
Metabolic, mineral, bone, and skeleton disorders – per event		
Hip fractures	-0.068	Sullivan et al.[10]
Other fractures		
Cancer – chronic disutility		
Renal cancer	-0.003	Sullivan et al.[11]
Urothelial cancer		
Acute kidney injury (AKI) – per event		
AKI – outpatient, hospitalization	-0.038	Sullivan et al.[10]
Adverse events – per event		
Leg amputation	-0.117	Peasgood et al.[12]
Toe amputation		
Foot amputation		
Liver injury	-0.080	Average of other-event related disutilities
Kidney Failure specific event - health state		
Immunosuppressive therapy	-0.010	Peasgood et al.[12]

Results

Base case

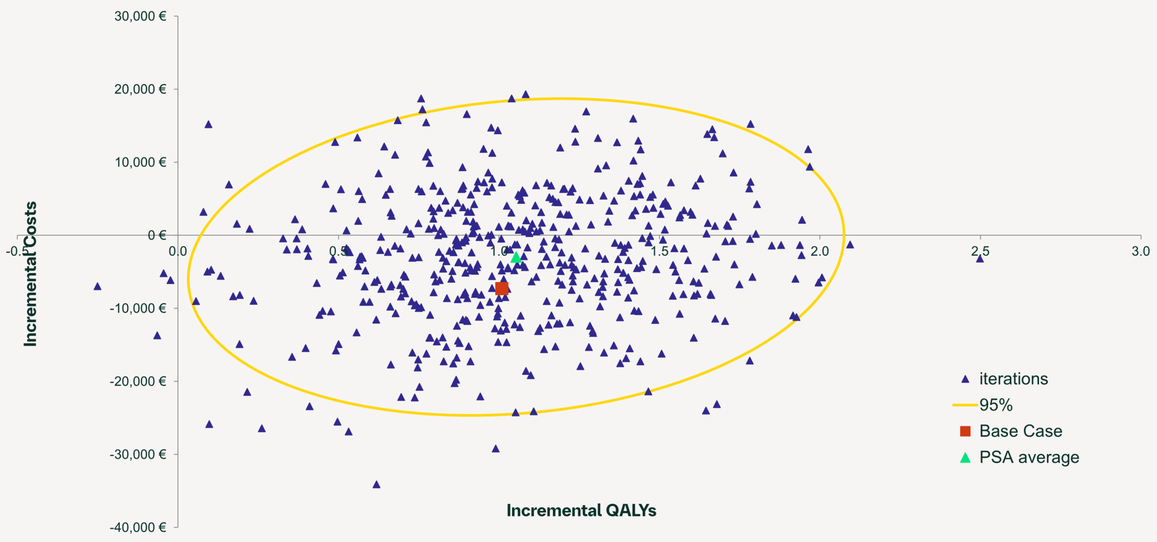
- Over a 25-year time horizon, by slowing disease progression and by delaying the time when patients are in KF, empagliflozin + SoC would increase the life expectancy of patients by **1.7 years**.
- The base case results showed total discounted costs of €159,423 for empagliflozin + SoC and €166,531 for SoC alone, **resulting in savings of €7,288** (Table 5).
- Empagliflozin + SoC was associated with higher total discounted QALYs, achieving 7.06 QALYs compared to 6.05 QALYs for SoC alone, **resulting in a dominant situation** (Table 5).

Table 5. Base case discounted cost-effectiveness results over a 25-years time horizon

	Empagliflozin + SoC	SoC	Incremental	ICER
Total discounted costs	€159,243	€166,531	€-7,288	-
Total discounted QALYs	7.06	6.05	1.01	**Dominant**

- A deterministic sensitivity analysis was conducted for 1,000 patients. **None of the parameters tested altered the dominant position of empagliflozin + SoC over SoC alone**. The two most impactful parameters were the annual cost of haemodialysis and the incremental treatment effects per health state during G4*A3 (15 < eGFR < 29 ml/min/1.73m² and uACR > 300 mg/g) in the SoC arm.
- A probabilistic sensitivity analysis estimated an average dominant result, with an incremental total cost of €-2,960 and an incremental gain of 1.05 QALYs. **The PSA results were consistent with the base case analysis, further confirming the robustness of Empagliflozin + SoC's dominance over SoC alone** (Figure 2).
- The quadrant distribution indicated that empagliflozin + SoC would dominate SoC alone in 62% of the simulations, would be more effective and more costly in 37% of the simulations and would be less effective and less costly in 1% of the simulations (Figure 2). **Empagliflozin + SoC would be 99% cost-effective at a willingness-to-pay threshold of €30,000**.

Figure 2. Probabilistic sensitivity analysis results



Sensitivity Analyses

- As detailed in the methods section, the assumptions made in the two sensitivity analyses did not affect the costs, only the QALYs. Since the incremental QALYs remained in favor of the empagliflozin + SoC arm in both scenarios, **the results were consistent with the base case analysis, reinforcing the robustness of empagliflozin + SoC's dominance over SoC alone** (Table 6).

Table 6. Total discounted QALYs over a 25 years time horizon in all scenarios

Scenarios	Empagliflozin + SoC	SoC	Incremental QALYs
Base case	7.06	6.05	1.01
Sensitivity analysis 1	7.32	6.26	1.05
Sensitivity analysis 2	7.00	5.99	1.00

Conclusions

Over a 25-year time horizon, this cost-effectiveness analysis demonstrated that empagliflozin + SoC in patients with CKD in France would significantly enhance life expectancy by slowing CKD progression and postponing the onset of KF, thus reducing the incidence of events and complications. Furthermore, **the base case indicated that empagliflozin + SoC would represent a dominant strategy compared to current SoC**, showing both superior outcomes and cost savings. Sensitivity analyses consistently confirmed this dominance, further strengthening these conclusions.

Abbreviations

CKD: Chronic Kidney Disease; eGFR: estimated glomerular filtration rate; HR: Hazard Ratio; ICER: Incremental Cost-Effectiveness Ratio; KDIGO: Kidney Disease: Improving Global Outcomes; KF: Kidney Failure; LYs: Life-Years; PSA: Probabilistic Sensitivity Analysis; QALYs: Quality-Adjusted Life-Years; SoC: Standard of Care; uACR: urine albumin-creatinine ratio

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Disclosures

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Romain SUPIOT managed the project on Putnam side and wrote the abstract. Jean TARDU managed the project on Boehringer Ingelheim side and proofread the abstract. Nicolas VIRELY, Marine SIVIGNON, and Anastasia USTER contributed to the analysis and proofread the abstract. Pierre LÉVY was consulted as an economic expert and proofread the abstract. Ziad MASSY was consulted as clinical expert to validate assumptions and key inputs of the model and proofread the abstract.

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