

# Cost-effectiveness of belatacept as conversion therapy in the management of patients living with a renal graft in France

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## Context

### Kidney transplantation

- Kidney transplantation (KT) is a life-saving procedure for patients with end-stage renal disease, providing substantially improved quality of life and survival compared to dialysis.
- The challenge in KT management is maintaining long-term graft function through effective immunosuppressive therapies. Tacrolimus is the most used calcineurin inhibitor (CNI), post KT. However, its use may lead to nephrotoxicity, potentially compromising graft survival.

### Belatacept

- Approved in France since 2021 as conversion therapy, belatacept offers an alternative immunosuppressive option for the prevention of KT rejection.

### French real-world study

- A French real-world study evaluated long-term outcomes in KT recipients converted from calcineurin inhibitors (CNIs) to belatacept-based regimens<sup>1</sup>. Among 311 patients enrolled (transplanted between 2007 and 2020; median follow-up of 5 years), conversion to belatacept was associated with a lower the risk of graft loss (GL) and an acceptable safety profile compared to continued CNI use.

## Objective

This study aims to evaluate the cost-effectiveness of belatacept as a conversion therapy in the management of adult kidney transplant patients in the French healthcare setting.

## Methods

### Model structure

- The base-case analysis simulated a cohort of 1,000 KT patients over a 15-year time horizon, applying an annual discount rate of 2.5%.
- A 7-state Markov model, adapted from the Peninsula Technology Assessment Group (PENTAG) model<sup>2</sup>, was used to compare belatacept and tacrolimus as maintenance therapies (Figure 1).
- Health states included functioning graft (FG), graft-loss (GL) and death with the possibility of up to two retransplantations per patient.

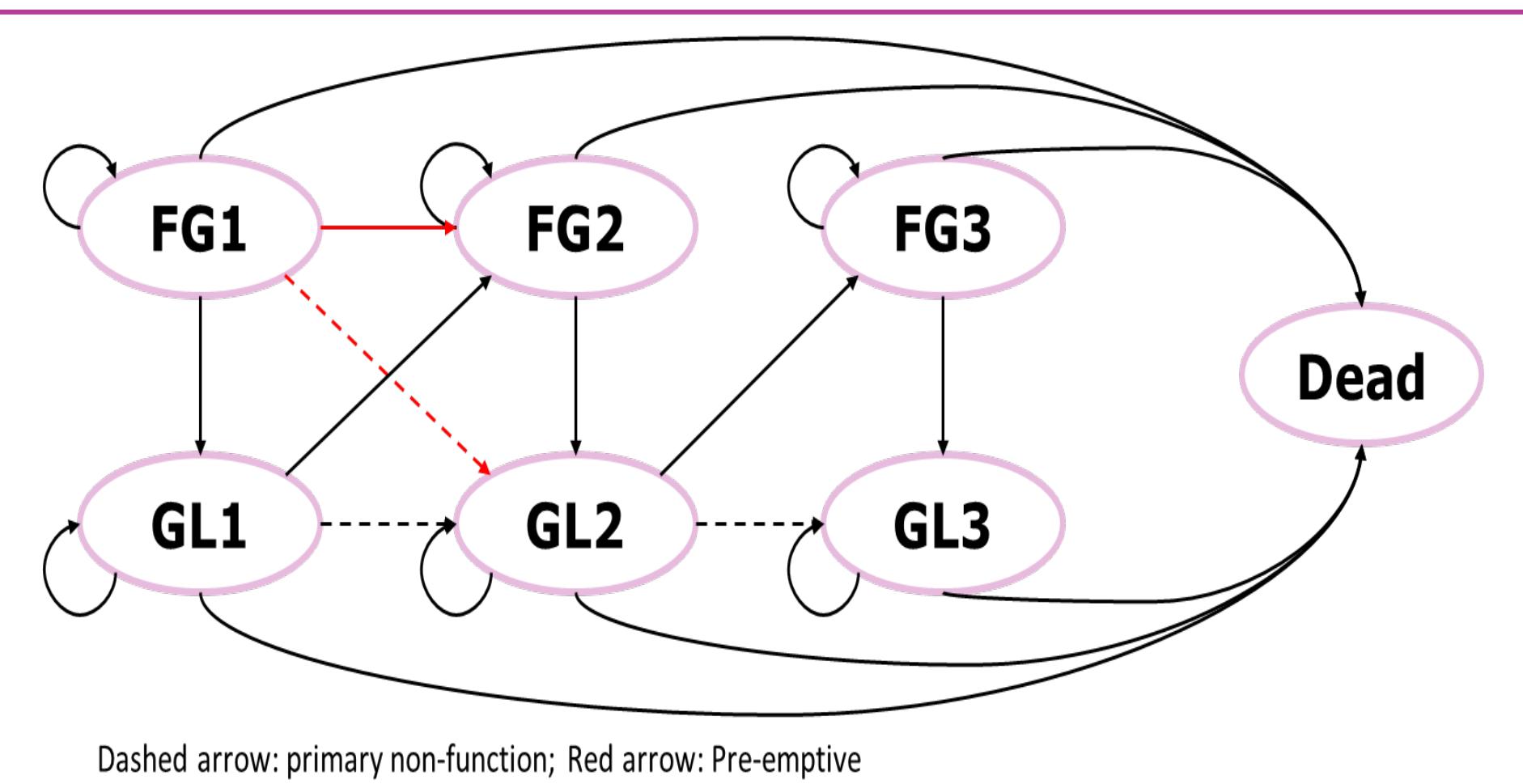


Figure 1. Model structure (7 health states)

### Efficacy data

- Graft survival 1 (GS1), defined as the time from transplantation to first graft loss for both comparators was extracted from the French real-world study published by Divard et al.<sup>1</sup> Lognormal distributions were selected as they provided the best statistical fit (Figure 2).

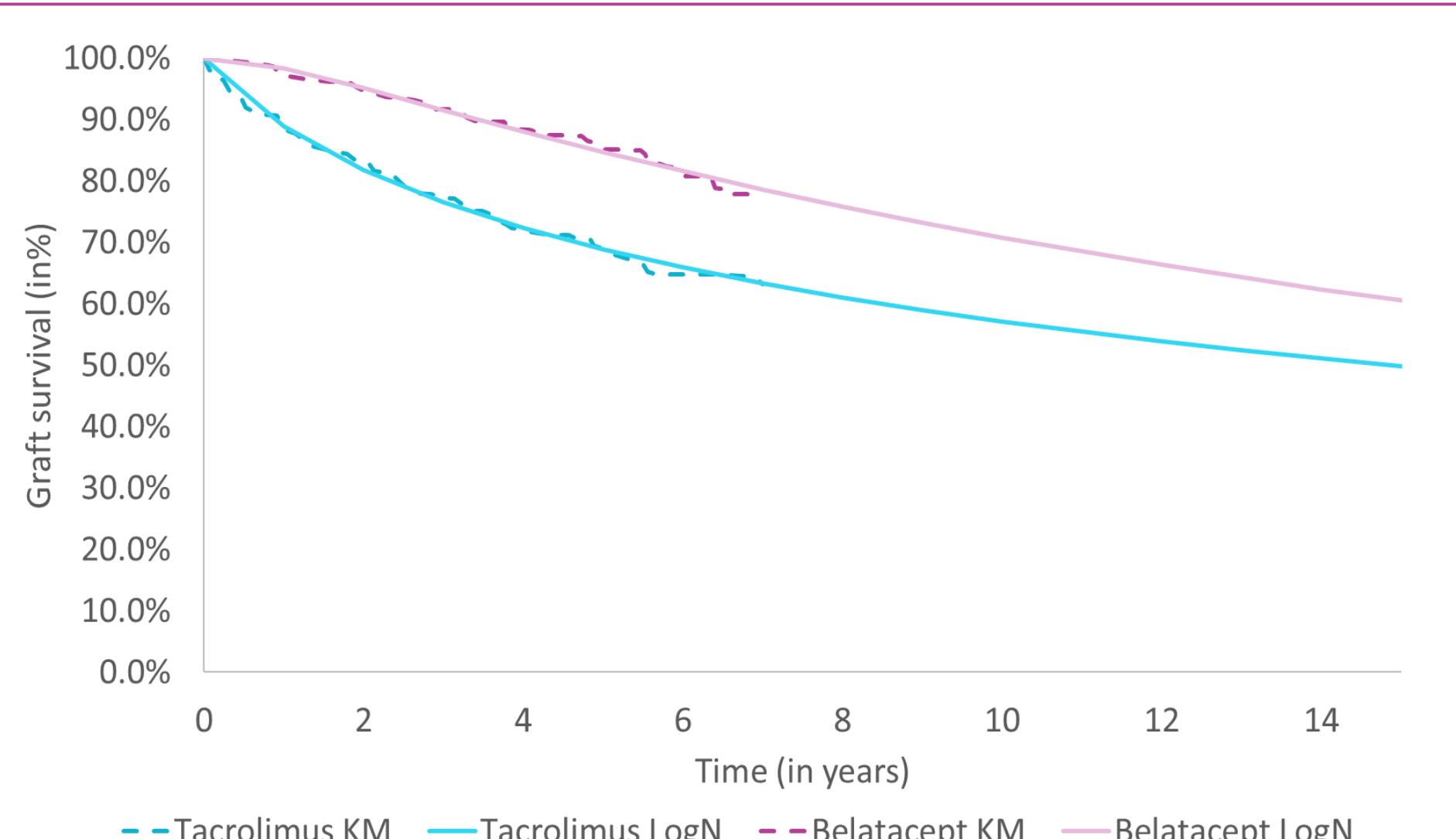


Figure 2. Kaplan-Meier curves and Log-normal distribution for tacrolimus and belatacept

- GS2 and GS3 were modeled using the exponential distribution based on tacrolimus survival graft 1, with the assumption of constant risk over the time horizon.
- Transitions probabilities including graft survival, death with functioning graft (DWFG) and death with graft loss were obtained from the literature (i.e French Agency of Biomedicine report<sup>3</sup>, UK Transplant Registry...).
- UK Transplant Registry standard data set was used to estimated DWFG1. For FG2 and FG3 states, a constant baseline mortality rate of 0.0078 was applied and adjusted, according to the long-running rate of DWFG1.

- Death with graft loss was assumed to be the same as mortality rates for dialysis from the French REIN 2022<sup>4</sup> report

### Utilities

- Health state utilities were estimated using EQ-5D-3L values derived from published literature<sup>5</sup>. General population utility score was assigned and disutilities were applied for functional graft status, hemodialysis, peritoneal dialysis, and new-onset diabetes after transplantation (NODAT)<sup>6</sup>.

### Costs

- A French healthcare system perspective was adopted for cost analysis. Included costs comprised treatment acquisition and administration costs, disease monitoring, health-states management (dialysis, graft loss, retransplantation), dialysis-related adverse events, patient transportation, and end-of-life care, based on hospital stay tariffs.
- According to national social security data, 50% of patients received belatacept at home infusion ("retrocession") while the remaining 50% were treated in hospital settings.

## Results

### Base case analysis

- Over a 15-year time horizon, belatacept was associated with an incremental survival gain of 0.34 years (+3.2%) and an increase of 0.47 QALYs (+5.6%) compared to tacrolimus (Table 1). Belatacept extended the time spent with a functioning graft and reduced the risk of first graft loss.

Table 1. Disaggregated discounted outcomes in the base case analysis

Outcomes	Belatacept	Tacrolimus	Difference
<b>Survival</b>			
Functioning graft	10.04	9.12	0.92 (+10%)
Graft loss	1.03	1.61	-0.58 (-36%)
Total Life years	11.07	10.73	0.34 (+3%)
<b>QALY</b>			
Functioning graft	8.35	7.54	0.81 (+11%)
Graft loss	0.58	0.92	-0.34 (-36%)
Total QALYs	8.93	8.46	0.47 (+5%)

- Belatacept increased acquisition and administration costs by €44,314 compared to tacrolimus (Table 2).
- By reducing the number of graft losses and time spent on dialysis, belatacept generated savings of €55,406.
- Savings associated with dialysis accounted for 79% of total savings (€70,547).
- Overall, belatacept resulted in savings of €24,921 per patient over a 15-year period compared to tacrolimus.

Table 2. Disaggregated discounted costs in the base case analysis

Costs (€2025)	Belatacept	Tacrolimus	Difference
<b>Treatment costs</b>			
Acquisition	101,750	83,720	18,030
Administration	26,284	0	26,284
Acquisition subsequent	8,365	14,776	-6,411
Administration subsequent	0	0	0
<b>Follow-up costs</b>			
Follow-up	27,167	25,854	1,313
<b>Health-states costs</b>			
Graft loss	3,774	5,469	-1,695
Dialysis	99,092	154,498	-55,406
Retransplantation	4,717	7,344	-2,627
<b>Adverse events costs</b>			
Functioning graft	4,095	6,569	-2,474
Dialysis	1,991	3,676	-1,685
<b>End-of-life costs</b>			
End-of-life	1,942	2,191	-249
<b>Total</b>			
	279,177	304,097	-24,921

- The belatacept strategy is both less expensive and more effective than tacrolimus, **thereby dominating the standard of care strategy**.
- Overall survival outcomes were validated using data from the French Biomedicine Agency<sup>3</sup>.

### Clinical events

- Treating 1,000 patients with belatacept would prevent 104 retransplantations and 157 cases of graft loss (Table 3).

Table 3. Clinical events avoided with the belatacept strategy

Events	Total number of events avoided per 1,000 patients	Confidence interval
Re-transplants	-104	[-107; -100]
Graft losses	-157	[-163; -151]
Deaths	-40	[-39; -36]

## Sensitivity Analyses

- Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) confirmed the robustness of the base case results.
- The most influential parameters were the cost of dialysis, time horizon, and average patient weight. In all scenarios tested, belatacept remained the dominant strategy compared to tacrolimus (Figure 3).

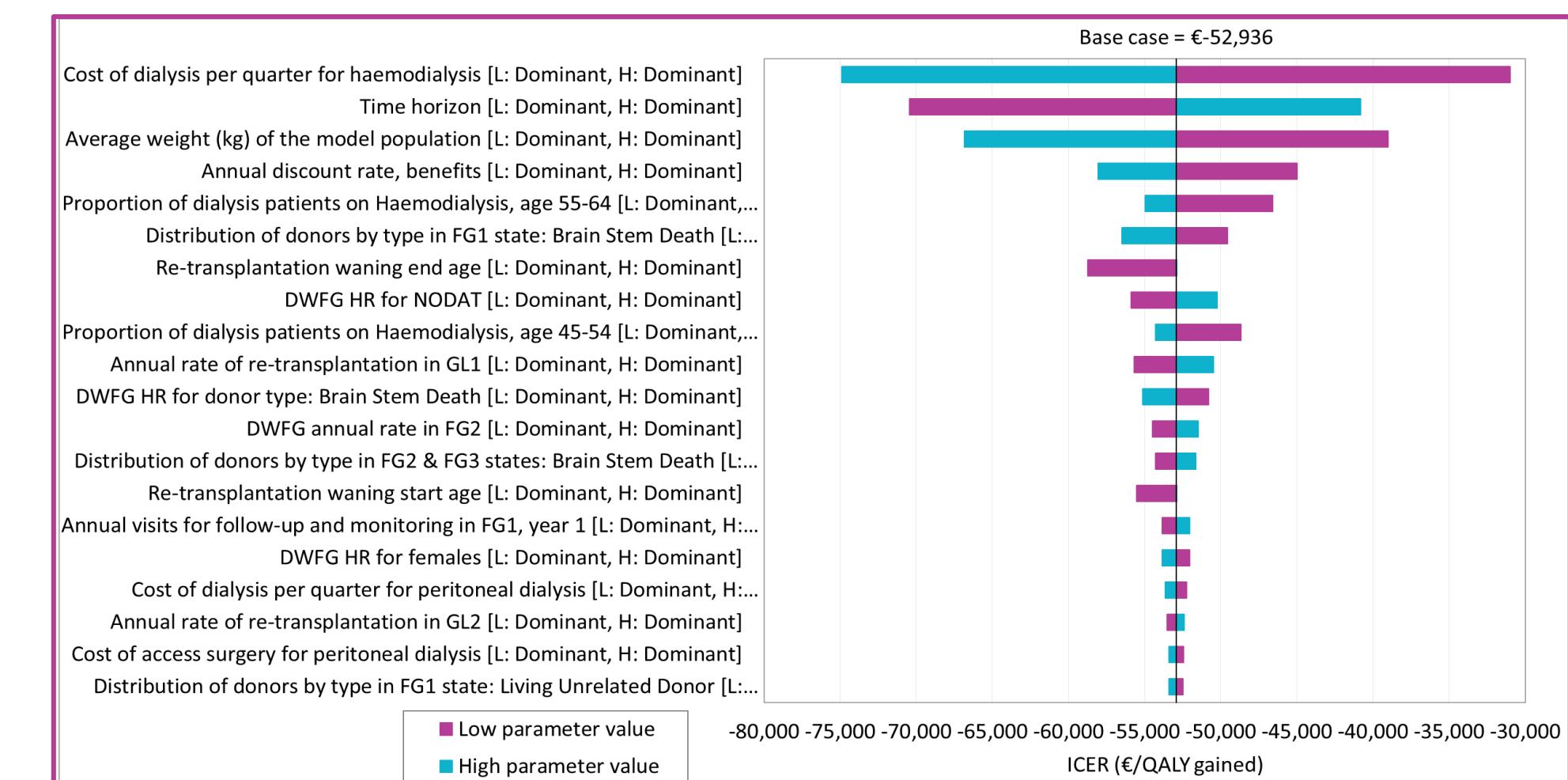


Figure 3. Tornado diagram

- Across 1,000 simulations, probabilistic sensitivity analysis (PSA) confirmed the dominance of belatacept, with an 80% probability of being the dominant strategy (Figure 4).



Figure 4. Incremental cost-effectiveness plane

## Scenario Analyses

Two scenarios for belatacept administration were evaluated to assess their impact on the cost-effectiveness results (Table 4):

- **Scenario 1** - 100% retrocession: This scenario results in greater cost savings compared to tacrolimus, with belatacept remaining the dominant strategy.
- **Scenario 2** - 100% hospital-based administration: All administrations occur in hospital settings. While cost savings are lower than with retrocession, belatacept still remains dominant over tacrolimus.

Overall, these alternative assumptions have a moderate impact on the results and do not alter the conclusion regarding the dominance of belatacept.

Table 4. Scenario analyses results

Scenario	Incremental Costs (variation vs. basecase in %)	Incremental QALY (variation vs. basecase in %)	ICER
Scenario 1 (100% retrocession)	-43,111 (+72%)	0.47	Dominant
Scenario 2 (100% hospital)	-6,731 (-72%)	0.47	Dominant

## Conclusion

Belatacept as conversion therapy for kidney transplant rejection prophylaxis is a dominant strategy in the French healthcare context.

Compared to tacrolimus, belatacept provides both cost savings and improved patient outcomes. By delaying graft loss, belatacept reduces dependence on dialysis and postpones retransplantation, resulting in better patient health and lower economic burden.

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