COST-EFFECTIVENESS ANALYSIS OF TEPROTUMUMAB VERSUS BEST SUPPORTIVE CARE FOR ACTIVE MODERATE-TO-SEVERE THYROID EYE DISEASE IN FRANCE

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INTRODUCTION

- Thyroid eye disease (TED) is an autoimmune disease affecting orbital tissues that occurs in 25% to 40% of patients with Graves' disease. Moderate-to-severe forms are rare but can lead to visual impairment.[1] The estimated incidence in Europe is approximately 5 per 100,000 individuals.[2]
- TED is a chronic condition that evolves over several years. It may be broadly divided into two phases: an inflammatory phase during which severe complications may occur (optic neuropathy, corneal ulcers, etc.) and a chronic phase during which reconstructive surgery may be considered.
- TED has a significant impact on patients' quality of life. Symptoms such as proptosis, diplopia and eye pain can limit patients' daily activities and ability to work and often lead to social and psychological difficulties. Many patients report psychological distress, appearance-related anxiety and an increased risk of depression.[3,4]
- Teprotumumab is the first human monoclonal antibody targeting the insulin-like growth factor 1 receptor (IGF-1R) to demonstrate reductions in proptosis and diplopia in patients with TED in four randomised, double-blind, placebo-controlled clinical studies, including OPTIC phase III trial in patients with active moderate to severe TED.[5]
- Teprotumumab has been available in France through a compassionate use program since 2021. In February 2026, the French National Authority for Health (HAS) issued a positive reimbursement opinion specifically for patients with active moderate-to-severe TED presenting with proptosis and/or diplopia.[6]
- According to European Thyroid Association (ETA) treatment recommendations, teprotumumab is a preferred therapy for patients with active moderate-to-severe TED presenting significant proptosis and/or diplopia.[7] In its reimbursement opinion, HAS therefore concluded that no clinical comparators exist for this indication.[6]

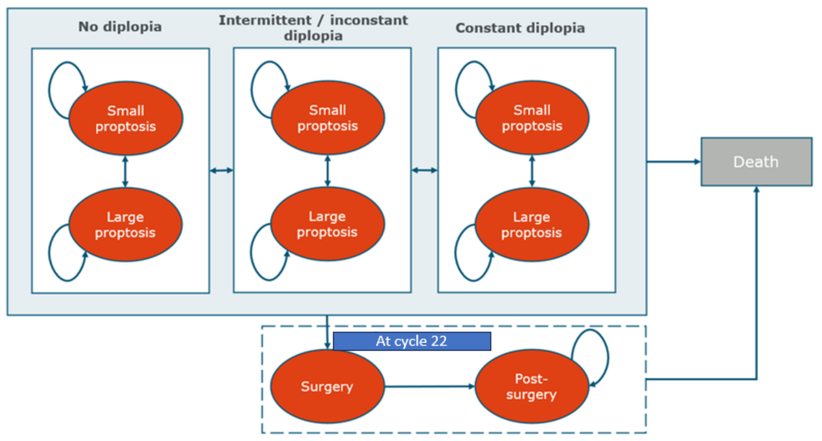
OBJECTIVE

- **This study assessed the cost-effectiveness of teprotumumab versus best supportive care (BSC) in France in patients with active moderate-to-severe TED presenting with diplopia and/or proptosis.**

METHODS

- Since TED is not associated with increased mortality, cost per year spent in the most favorable health state (small proptosis, no diplopia [SPND]) was used instead of cost per life-year (LY) to estimate an incremental cost-effectiveness ratio (ICER).
- A nine-state Markov model extrapolated clinical outcomes, quality of life and treatment-related costs for patients with active moderate-to-severe TED receiving teprotumumab versus BSC over a 20-year time horizon. Six health states represented combinations of diplopia and proptosis severity in TED. The additional health states were surgery, post-surgery and death (Figure 1).

Figure 1: Structure of the Markov model



- **Best Supportive Care (BSC), defined as a watch-and-wait strategy, was the only comparator included** in the model, in line with the ETA recommendations [7] and the HAS reimbursement opinion [6].
- **Efficacy, measured by proptosis reduction and diplopia improvement, was estimated directly from OPTIC phase III data.** Transition probabilities between health states were derived for both arms using patient-level OPTIC data.[5] Consistent with the natural history of the disease, a proportion of patients were assumed to be at risk of relapse, potentially leading to a recurrence or worsening of symptoms.
- **Transition to surgery** is possible in both arm from month 30, a period that includes the active phase and the time required for symptoms to stabilize after surgery, onward, from all disease-related health states. The transition probabilities to surgery for each health state are based on the natural history of the disease and expert opinion. These probabilities are the same in both treatment arms in the analysis.
- **No grade 3 or higher treatment related adverse events were reported in the OPTIC** phase III clinical trial; therefore, they are not included in the model.
- **No subsequent treatments are included**, apart from surgery.

RESULTS

- Compared with BSC, teprotumumab increased time spent in the most favorable health state by 2.3 years (6.98 vs. 4.68 years) and generated an incremental cost of €131,984 (€148,783 *vs.* €16,799) over a 20-year time horizon. The ICER was €57,341 per Life Year Gained in the Most Favorable Health State (LY MFHS) (Table 1).

Table 1: Total costs, life-years and QALYs

Intervention	Total costs (€)	Total LY	Total LY MFHS	ICER (€/LYG MFHS)
teprotumumab	148,783€	15.3	6.98	€57,341 LYG MFHS
Active surveillance	16,799€	15.3	4.68	
Difference	131,984€	0	2.3	

- Total costs in the most favorable health states were generally higher in the teprotumumab arm than in the BSC arm. Some patients achieved symptom reduction more quickly while still receiving treatment. In contrast, BSC involved no treatment acquisition or administration costs. Table 2 shows the cost breakdown by health state.
- Teprotumumab generated savings mainly in post-surgery costs (-€3,998), surgery costs (-€1,159) and costs in the large proptosis, constant diplopia health state (-€611). Surgical cost savings were attributed to a lower likelihood of orbital and strabismus surgery during the chronic phase, following reductions in proptosis and diplopia with teprotumumab during the active phase (surgery probability being higher in less favorable health states).

Table 2: Cost breakdown (main analysis)

Cost item	Teprotumumab	BSC	Difference
Total	**€148,783**	**€18,799**	**€131,984**
Small proptosis, no diplopia (SPPD)	€79,451	€1,038	€78,450
Large proptosis, no diplopia (LPND)	€23,821	€1,480	€22 783
Small proptosis, intermittent/inconstant diplopia (SPID)	€26,598	€2,776	€25 118
Large proptosis, intermittent/inconstant diplopia (LPID)	€5,475	€1,085	€2 699
Small proptosis, constant diplopia (SPCD)	€9,785	€1,652	€8 700
Large proptosis, constant diplopia (LPCD)	€1,041	€1,972	- €611
Surgery	€813	€5,796	- €1 159
Post-surgery	€1,788	€5,796	- €3 998

SENSITIVITY AND SCENARIO ANALYSES

- **The deterministic sensitivity analysis** (67 parameters tested) showed that the parameters with the greatest impact on the ICER were the proportion of patients with proptosis relapse in the teprotumumab arm, the proportion with diplopia relapse in both arms, and the transition probability from the LPCD health state in the teprotumumab arm (Figure 2). ICER variations did not exceed ±10% (€51,606 to €63,075) for the other parameters tested.
- **The cost-effectiveness acceptability** curve shows that teprotumumab versus BSC has an 80% probability of being cost-effective at a willingness-to-pay threshold of €80,000 per LYG MFHS (Figure 4).

Figure 2: Tornado diagram

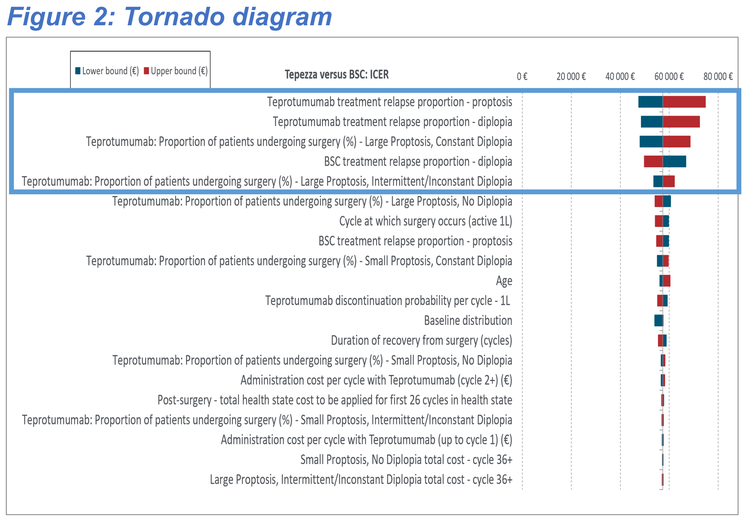
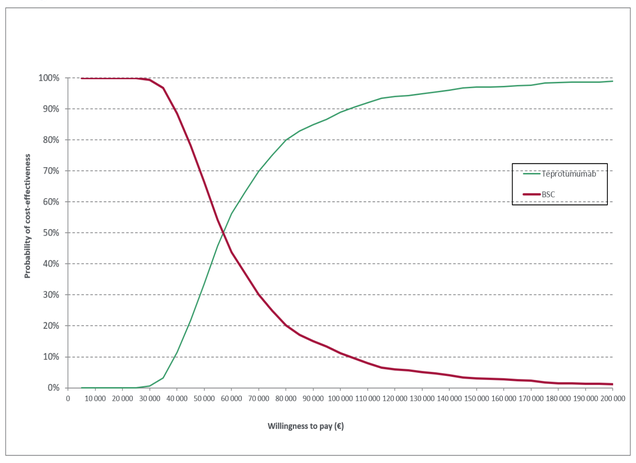
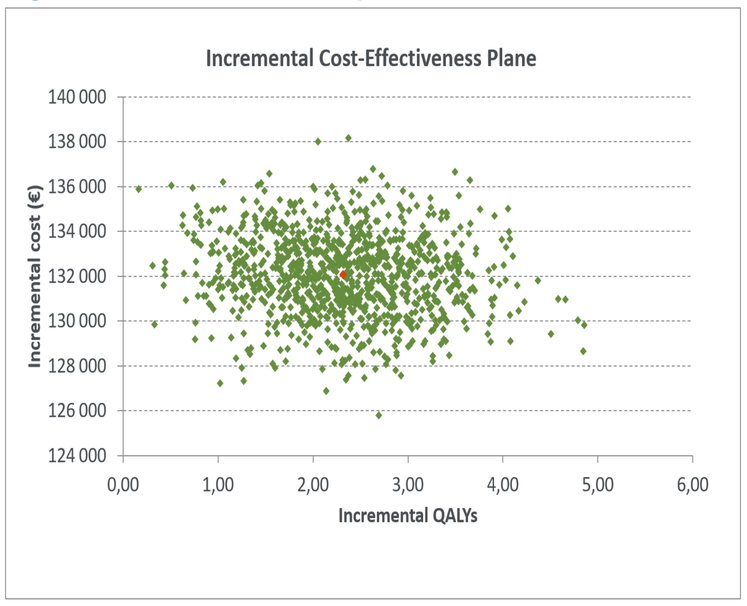


Figure 4: Acceptability curves



- **Several scenario analyses** were also conducted. The scenarios with the greatest impact on the ICER were:
  - Reduction of the time horizon to 15 years (€67,866/LY MFHS, +18%)
  - Lifetime horizon (€33,150/LY MFHS, -42%)
  - Exclusion of relapses (€35,043/LY MFHS, -39%)
  - Decrease in the adherence rate from 100% to 80% (€46,403/LY MFHS, -19%)
  - Discount rate for costs and health benefits set to 4.5% instead of 2.5% (€65,221/LY MFHS, +14%)
  - Discount rate for costs and health benefits set to 0.0% instead of 2.5% (€47,603/LY MFHS, -17%)
- **In the probabilistic sensitivity analysis (PSA),** teprotumumab was more effective and more costly than BSC in all simulations (1,000 iterations), with a mean probabilistic ICER of €56,998 per LYG MFHS (Figure 3).

Figure 3: Cost-effectiveness plane



CONCLUSIONS

- This cost-effectiveness analysis shows that alternative outcomes specific to disease progression may help overcome data scarcity in a rare disease setting. A life-year gained in the SPND health state appears to be a relevant outcome measure, given the symptom improvements observed directly in clinical trials.
- Despite the model's sensitivity to parameters related to surgery and relapse, the consistency of results across the sensitivity analyses supports its overall robustness.
- **From both French healthcare and societal perspectives, teprotumumab may be a cost-effective option compared with best supportive care (BSC) for patients with active, moderate-to-severe thyroid eye disease (TED) presenting with proptosis, diplopia, or both. Its economic value in France should be reassessed following final price negotiations.**

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