Cost-Utility of Acromegaly second line pharmacological treatments in adult patients in France (2023)

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BACKGROUND

The Cost-utility of second-line Acromegaly treatments in France has already been assessed in 2021 in a previous paper " Cost-utility of Acromegaly Pharmacological Treatments in a French Context" [a].

Acromegaly is a rare disease characterized by progressive somatic disfigurement (mainly involving the face and extremities). and systemic manifestations due to organ overgrowth related to excessive production of growth hormone (GH) [b].

Overproduction of GH results in increased levels of insulin-like growth factor 1 (IGF-1). Prolonged exposure to IGF 1 is associated with worsening of comorbidities. poorer quality of life and increased mortality risk [c].

OBJECTIVE

The purpose of this new analysis is to assess the efficiency of second-line drug therapy [pegvisomant, pasireotide, and pegvisomant combined with First Generation Somatostatin Analogues (FGSA)], considering the results of first-line treatments (surgery, FGSA, cabergoline and combinations) and radiotherapy to better describe the global patient care pathway.

Treatment efficacy is defined on both normalization of IGF-1 and effect on tumor volume (the last parameter was not considered in the first analysis).

METHODOLOGY

- The prior 3-state Markov model has been revised to include an additional health state. representing patients who are controlled without pharmacological treatment following successful radiotherapy [Figure 1] .
- The model accounted for the history of first-line treatments as additional costs for patients upon entry.
- A cohort of 1.000 simulated patients was followed over a lifetime horizon corresponding to a simulation period of 45 years (versus 40 years in the first analysis)
- The analysis was performed from a French collective perspective

Clinical inputs :

- The median age at diagnosis was 45.2 years old.
- Patients enter the model as uncontrolled after failure of 1st line treatment
- Treatment history corresponding to each state is summarized in Table 1.

Table 1 : First line treatment history for each state

First line treatment history	PASIREOTIDE	PEGVISOMANT +/- FGSA
FGSA only	33%	13.1%
FGSA → FGSA + Cabergoline	8.7%	13.1%
Surgery → FGSA	35.3%	52.6%
Surgery → FGSA → FGSA + Cabergoline	20.0%	18.2%
Surgery → Cabergoline → FGSA + Cabergoline	3.0%	3.0%
	Petersen et al.	*ACROSTUDY*

- A network meta-analysis inferred the efficacy of 2nd line treatments.
- Treatment effects were assessed every 12 weeks until the end of the 1st year for each arm. Beyond that time, no treatment effect was assumed for the remainder of the time horizon. The duration of subsequent cycles was set at 1 year.
- Radiotherapy is used as a proxy for tumor volume control for pasireotide and pegvisomant. More specifically, Pasireotide enables better control of tumor volume and avoids the need for radiotherapy.
- Adverse events (AE) associated to treatment were included in the model.

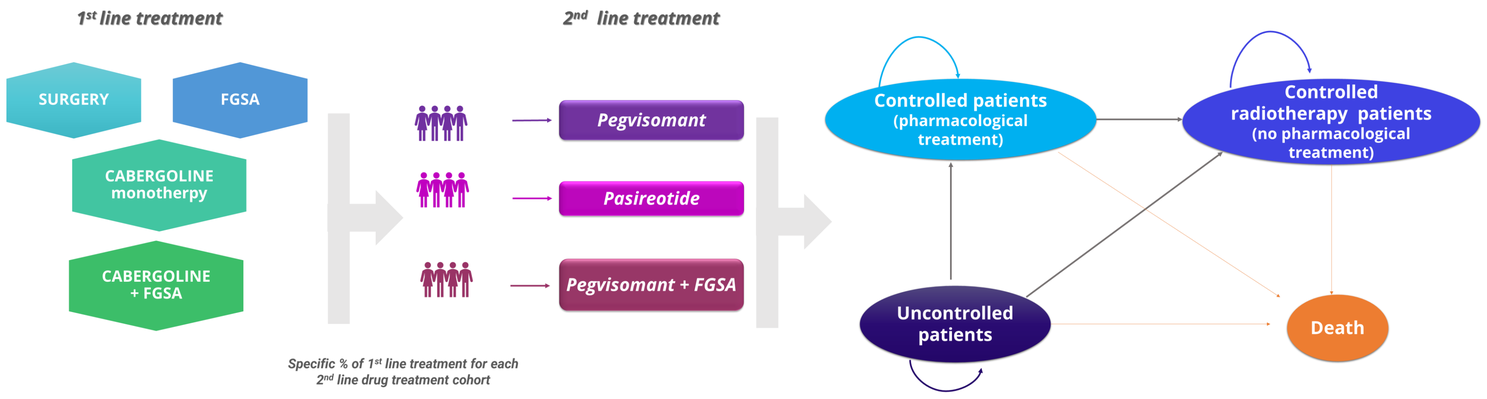
Mortality :

- Probability of death depends on the age and gender and the health state
- Standardized Mortality Ratio (SMR) [d] : Controlled = 1.10 vs Uncontrolled = 2.50

Included costs

- Surgery costs
- Drug acquisition costs
- Drug administration costs
- Health states costs
- Radiotherapy costs
- AE management & comorbidity costs
- Monitoring costs
- Societal costs (productivity loss) : Exploratory

Figure 1 : Model structure



Health-related Quality of Life

- Instrument : the EQ 5D index value
- Controlled : values of general French population norms [e] .
- Uncontrolled : utility decrement of 20.5% applied on general French population [f] .

Table 2 : Utility data

Treatments	Controlled	Uncontrolled
45-54 years old	0.922	0.733
55-64 years old	0.853	0.678
65-74 years old	0.810	0.644
75 + years old	0.735	0.584

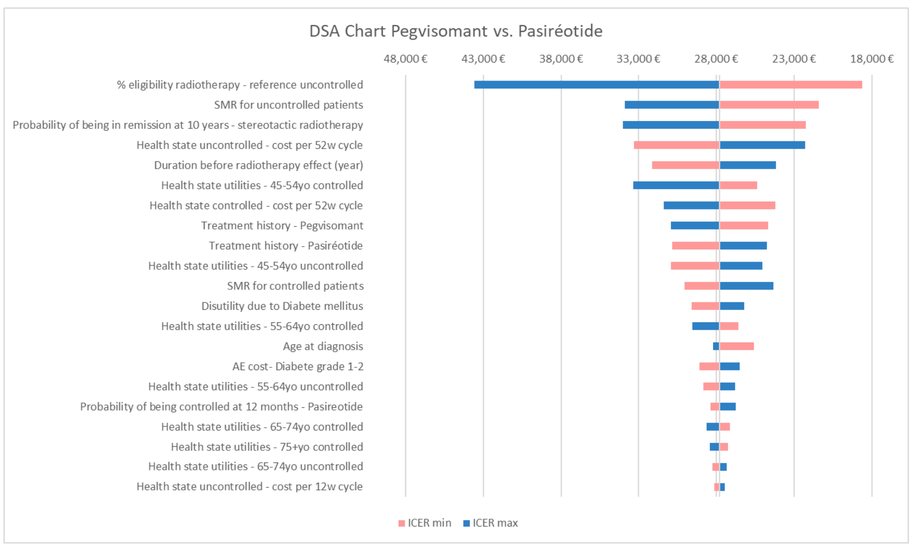
RESULTS

Pegvisomant was associated with higher incremental Quality-Adjusted-Life- Years (QALY) resulting in an incremental cost-utility ratios (ICUR) of 27.804.89 €/QLAY and 253.854.14 €/QALY versus pasireotide and the association of pegvisomant and FGSA, respectively. [Table 3].

Table 3 : Base Case Results

Costs over 45 years	Pasireotide	Pegvisomant	Pegvisomant + FG SA
Total costs	**1.060.673.26 €**	**1.134.306.00 €**	**1.185.856.86 €**
History costs	40.306.07 €	41.583.65 €	41.583.65 €
Drug acquisition costs	785.668.54 €	908.055.37 €	959.614.18 €
Administration costs	1.910.14 €	7.25 €	2.155.48 €
Monitoring costs	5.348.56 €	3.954.69 €	3.656.58 €
AE related costs	17.626.42 €	267.83 €	11.25 €
Health state costs	206.051.11 €	178.709.20 €	177.194.14 €
Radiotherapy costs	3.758.55 €	1.724.50 €	1.597.19 €
End of life costs	3.87 €	3.51 €	3.50 €
Life years (LY)	22.90	23.75	23.79
QALY	16.44	19.09	19.29
ICUR (€ / QALY)	**-**	**27.804.89 €**	**253.854.14 €**

Figure 2 : DSA Tornado plot



The deterministic sensitivity analysis (DSA) showed that the model results were most sensitive to variation of % of uncontrolled patients eligible to radiotherapy, SMR for uncontrolled patients and probability of remission at 10 years [Figure 2].

The probabilistic sensitivity analysis (PSA) run with 1000 simulations, showed that pasireotide was less costly but also less effective than other strategies.

CONCLUSION

The updated model aims to offer a more thorough and comprehensive view of the cost-utility of second-line pharmacological treatments in acromegaly. Beyond clinical data, this analysis broadens our perspective within a framework where costs of treatments are rising, and healthcare system financing is more challenging. Treatment with Pegvisomant resulted in improved health outcomes and increased cost compared to pasireotide. Though, patients under Pegvisomant, were better controlled and therefore do not require radiotherapy. However, the association of pegvisomant and FGSA was more expansive with limited improvement of health outcomes.

REFERENCES

a. *Cost-Utility of Acromegaly Pharmacological Treatments in a French Context [DOI : 10.3389/fendo.2021.745843]*
b. *Orphanet*
c. *Challenges in the diagnosis and management of acromegaly: a focus on comorbidities [DOI : 10.1007/s11102-016-0725-2]*
d. *Holdaway et al. 2008*
e. *Janssen et al. 2016*
f. *Rowles et al.2005*

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