EE358

EFFICIENCY OF THIRD-GENERATION ANTISEIZURE MEDICATIONS IN SPAIN FOR DRUG-RESISTANT EPILEPSY:

A COST-PER-NUMBER NEEDED TO TREAT ANALYSIS

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BACKGROUND AND OBJECTIVES

- The main goal of epilepsy treatment is to achieve **seizure freedom** without intolerable adverse effects. However, approximately **40% of patients with epilepsy** continue to experience seizures (mainly focal-onset seizures (FOS)), despite treatment with at least two antiseizure medications (ASMs) suffering **drug-resistant epilepsy** (DRE) [1]. This represents **more than 50,000 patients with DRE in Spain** [2,3]**.**
- The most recent ASMs approved for FOS in the last decade are brivaracetam, perampanel, lacosamide and eslicarbazepine acetate (the so-called **"third-generation ASMs"**), which represent the **most commonly prescribed options** in DRE patients. **Cenobamate is a new ASM and the first one approved and reimbursed in Spain (July 2022) for the adjunctive treatment of FOS in adult patients with DRE** [4].
- The introduction of a new ASM increases the number of therapeutic options available, making it important to compare the new drug with existing alternatives to be able to **determine its relative clinical benefit taking into account its cost**. The **number needed to treat (NNT)** offers a measurement of the impact of a medicine by estimating the number of patients that need to be treated in order to have an impact on one person [5].
- **The aim of this study is to determine the efficiency, in terms of cost per NNT, of third-generation ASMs for the adjunctive treatment of FOS in patients with DRE in Spain.**

METHODS

- NNT data (*Figure 1*) were calculated based on the seizure freedom endpoint (defined as the percentage of patients achieving 100% reduction in seizure frequency from baseline), obtained from pivotal clinical trials performed with cenobamate, brivaracetam, perampanel, lacosamide and eslicarbazepine acetate. The NNT was established as the inverse of the treatment responder rate minus the placebo responder rate, according to the following formula [5]:

$$NNT = \frac{1}{\pi_1 - \pi_0}$$

π0: risk control group; π1: risk in treatment group

- The cost of each ASM was calculated both based on the mid-range dose and maximum dose studied in their pivotal clinical trials (*Table 1*) [6-10]. The pharmacological costs were obtained from the BotPlus database [11] after applying the compulsory 7,5% discount for each drug (except for eslicarbazepine acetate and lacosamide, for which the deduction is not applicable) in accordance with Spanish legislation (RDL 8/2010) [12].
- The cost per NNT (CNT) (*Figure 2*) for each ASM was calculated by multiplying its annual treatment cost by its NNT values.

Table 1: ASM Daily doses studied in pivotal clinical trials

ASM	Posology (mg/day)	
	Mid-range dose (DDD)	Maximum dose
Cenobamate	200	400
Brivaracetam	100	200
Perampanel	8	12
Lacosamide	400*	600
Eslicarbazepine acetate	800	1,200

**All mid-range doses of ASMs correspond to their DDD, except for lacosamide.*

RESULTS

- NNTs values ranged between 10 and 60 when calculated based on DDDs. **Cenobamate** represents the **most effective ASM** associated with **the lowest NNT (10).** Its differences in NNT values with respect to the alternatives were between 2 to 6 times lower.
- NNT values ranged between 5 and 33 when calculated based on maximum doses. Likewise, **cenobamate was associated with the lowest NNT (5).** Differences with the other ASMs were higher in this case and between 4 and 6 times lower.
- When considering **DDD**, the **most efficient ASM was cenobamate**, followed by brivaracetam, eslicarbazepine acetate, lacosamide and perampanel, with CNT values ranging from 13,181€ (cenobamate) to 49,773€ (perampanel).
- When considering **maximum dose, cenobamate** was also **the most efficient ASM**, followed by eslicarbazepine acetate, brivaracetam, lacosamide and perampanel, with CNT values ranging from 13,451€ (cenobamate) to 46,126€ (perampanel).

Figure 1: NNT values for Seizure freedom for each ASM

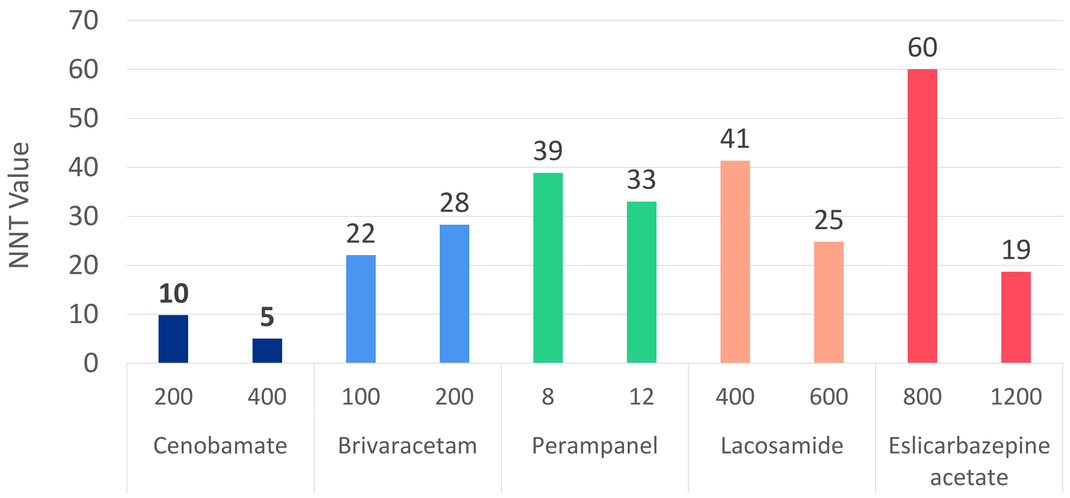
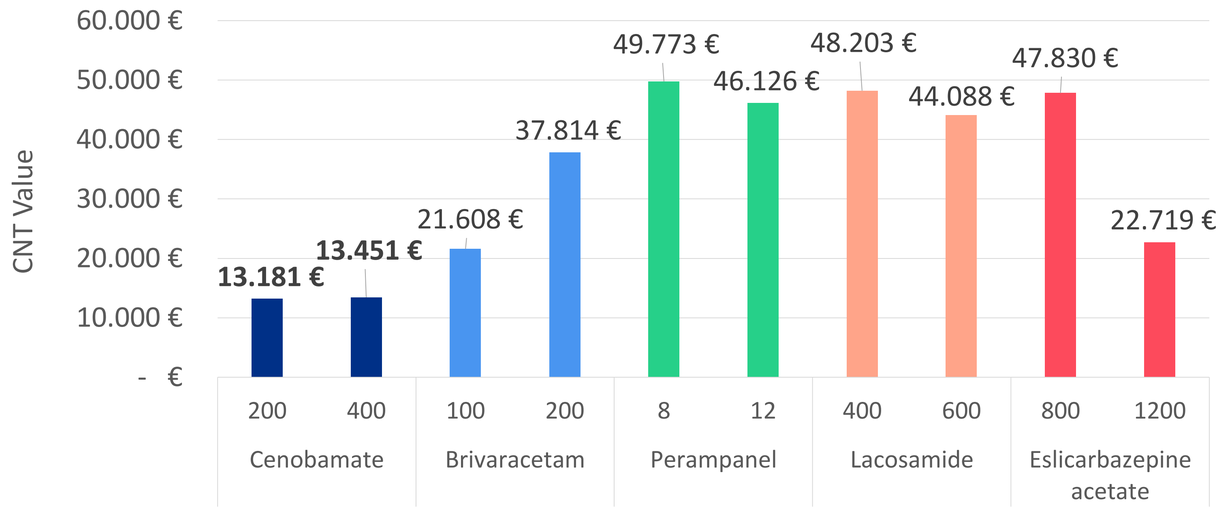


Figure 2: Annual CNT values for Seizure freedom for each ASM



CONCLUSIONS

The findings show a clear link between the efficacy of third-generation ASMs available in Spain for the treatment of FOS in patients with DRE and their efficiency, facilitating determination of drug's value contribution and decision-making in Spain.

Cenobamate presents the lowest cost per NNT relative to seizure freedom, proving to represent the most efficient option compared to third-generation alternatives.

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