M403

Cost-Effectiveness Analysis of Non-invasive Vagus Nerve Stimulation for the Treatment of Chronic Cluster Headache in Germany

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Introduction

- Chronic cluster headache (CH) is a debilitating condition that can negatively impact quality of life (QoL)[1]
- CH is associated with substantial healthcare costs, including both direct (eg, medication and clinic visits) and indirect (eg, reduced working capacity) costs[2]
  - The costs of abortive medications can be 2-fold higher for patients with chronic CH than for those with episodic CH[2]
- Results from the PREVA study[3] demonstrated that treatment with a novel non-invasive vagus nerve stimulation (nVNS) device (gammaCore®; **Figure 1**) decreased abortive medication use and improved QoL outcomes in subjects with chronic CH
- To quantify the economic impact of nVNS therapy in patients with chronic CH, we developed a pharmacoeconomic model using data from the PREVA study

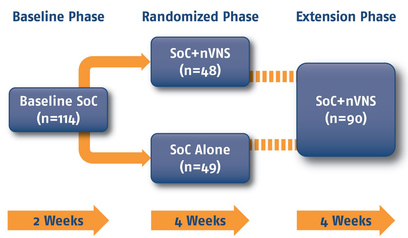
Figure 1. nVNS Device

Methods

PREVA Study Design

- PREVA evaluated the safety and efficacy of adjunctive nVNS therapy compared with subjects' standard of care (SoC) alone (**Figure 2**)
- Subjects delivered 3 mandatory, prophylactic 120-second stimulations to the right side of the neck twice daily
  - Delivery of additional stimulations as acute treatment of CH attacks was optional

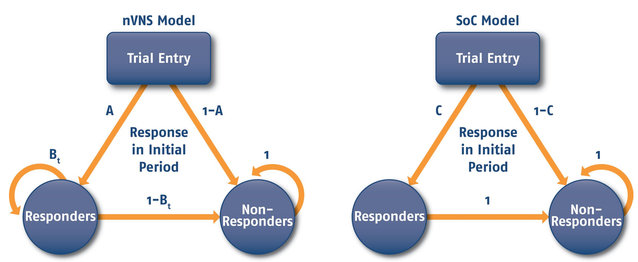
Figure 2. PREVA Study Design



Pharmacoeconomic Model Development

- A 1-year model (**Figure 3**) estimated the cost-effectiveness of adjunctive nVNS therapy from the German Statutory Health Insurance perspective
  - Benefits were defined as quality-adjusted life-years (QALYs)
  - Healthcare utilization costs were estimated from abortive medication use and the cost of the nVNS device
- Model parameter estimates were derived using efficacy and abortive medication use data from the randomized phase of the PREVA study
  - Data from the extension phase were used to generate a survival analysis to extend the model to 12 months

Figure 3. Model Structure



A = probability of response in the nVNS+SoC group; B_t = probability of maintaining response in the nVNS+SoC group; C = probability of response in the SoC group.

Estimating Treatment Response and Maintenance of Response

- *Treatment response* was defined as >50% reduction from baseline in the number of CH attacks
  - SoC treatment responders were modeled as nonresponders beyond the randomized phase
  - Subjects from the nVNS+SoC group who responded through the extension phase were assumed to maintain this response
- These assumptions were modified in alternative scenarios to test the sensitivity of the model

Estimating QALYs

- QALYs for both groups were estimated using the EQ-5D™ index data from the randomized phase in an ordinary least squares regression analysis

Estimating Healthcare Utilization and Costs

- Abortive medication use data from the last 14 days of the PREVA randomized phase were used to assess healthcare utilization
- The nVNS unit cost was the listed price in Germany
- Intranasal (IN) zolmitriptan and subcutaneous (SC) sumatriptan unit costs were determined from the German pharmaceutical directory, Rote Liste®
- Unit costs for inhaled oxygen canisters were estimated from a previously published treatment cost study[2]

Results

Parameter Estimates

- The probability of response was greater in the nVNS+SoC arm (0.49) than in the SoC alone arm (0.09)
- The frequency of abortive medication use by both groups is presented in **Table 1**
- Unit costs of abortive medications and nVNS are presented in **Table 2**

Table 1. Number of Times Abortive Medications Were Used During the Last 14 Days of the Randomized Phase

Abortive Medication	nVNS+SoC (n=33)*	SoC Alone (n=46)*
IN zolmitriptan	1.6 (5.5)	1.3 (3.6)
SC sumatriptan	2.7 (4.0)	7.7 (9.8)
Inhaled oxygen	6.5 (10.9)	11.1 (14.9)

Data are presented as mean (SD). *n Values represent any subject who reported using an abortive medication.

Table 2. Unit Cost of Treatments

Treatment	Description	Cost/Dose (€)
IN zolmitriptan	AscoTop® Nasal 5 mg/Dosis Nasenspray, Solution: €90.63; 6 single-dose nasal sprays	15.11 (90.63 ÷ 6)
SC sumatriptan	Sumatriptan-Hormosan® Inject 6 mg/0.5-mL Solution: €199.92; 6 prefilled syringes	33.32 (199.92 ÷ 6)
Inhaled oxygen	Inhaled oxygen: €2.93 per day in CH patients[2]	2.87 (2.93 ÷ 1.02 uses per day)
nVNS	gammaCore: €375.00; loaded with 150 stimulations	2.50 per stimulation (375 ÷ 150)

Since completion of this analysis, a gammaCore device loaded with 300 stimulations has been made available in the European Union for €454.00 (€1.51 per stimulation).

Cost-Effectiveness Analysis

- Abortive medication costs were 30% lower in the nVNS+SoC group than in the SoC alone group (**Figure 4**)
  - Compared with the SoC alone group, the nVNS+SoC group had 36% lower sumatriptan costs, 39% lower inhaled oxygen costs, and 85% higher IN zolmitriptan costs
- Estimated costs and mean QALY per subject are shown in **Table 3**
- The incremental cost-effectiveness ratio, or the expense of gaining an additional QALY with adjunctive nVNS therapy, was €4,746
  - This falls well below the €20,000 per QALY gained that commissioners of healthcare services are willing to pay for new technologies[4]
- Altering the model by increasing or decreasing the likelihood of loss of response in either group had little effect on the cost-effectiveness ratio

Figure 4. Breakdown of Modeled 1-Year Abortive Medication Costs by Category

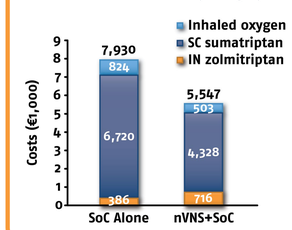


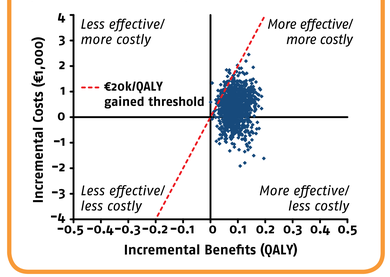
Table 3. Total Costs and QALYs From the 1-Year Model

Treatment Arm	Mean Costs (€)	Mean QALYs
nVNS+SoC	8,346	0.620
SoC alone	7,930	0.532

Probabilistic Sensitivity Analysis

- The model was replicated 1,000 times to determine its certainty (**Figure 5**)
  - All plots fell to the right of the vertical axis, indicating that nVNS is more effective than SoC
  - ~25% of the plots fell in the southeast quadrant, suggesting nVNS has potential to reduce costs
  - More than 95% of plots fell below the €20,000/QALY gained threshold[4]

Figure 5. Scatterplot of Base Case Model Simulations (Cost-Effectiveness Plane)



Conclusions

- **Data from the PREVA study suggest that adjunctive nVNS therapy may reduce the need for abortive medications and improve QoL in patients with chronic CH**
- **Pharmacoeconomic analyses suggest that nVNS is a highly cost-effective treatment**
  - **Considering additional healthcare costs that were not included in the model (eg, clinic visits), nVNS therapy may likely promote further cost savings**
- **This study provides evidence of the efficacy and economic benefits of nVNS therapy for patients with chronic CH, which may be valuable information for doctors, patients, and payors**

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