CLINICAL AND ECONOMIC OUTCOMES OF MICROINVASIVE GLAUCOMA SURGERY (MIGS) WITH STENTS IN PATIENTS WITH MILD-TO-MODERATE OR REFRACTORY GLAUCOMA IN SPAIN

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INTRODUCTION

- Glaucoma is an incurable, chronic neurodegenerative disease often caused by high intraocular pressure (IOP) that may lead to permanent blindness.
- Its prevalence is 2.1% (99% CI, 1.9-2.3%) in the Spanish population [1, 2].
- Reducing IOP is the only treatment approach to slow the progression of glaucoma.
- Annual cost per patient varies from €810 (mild glaucoma) to €1,196 (severe glaucoma) in Europe, with medications being the key cost driver [3, 4].
- Microinvasive glaucoma surgery (MIGS) with stents is a treatment alternative that controls IOP by improving the drainage of aqueous fluid. MIGS avoid conjunctival dissection wherein stents are implanted via an ab interno incision [5].
- Evidence on the cost associated with MIGS surgery and follow-up healthcare resource utilization due to reduction in IOP and adverse events (AEs) may be helpful to inform treatment selection.

OBJECTIVE

To review clinical evidence and estimate annual cost of MIGS with stents in mild-to-moderate or refractory glaucoma from a Spanish hospital perspective.

METHODS

Clinical Review

- **Type of studies:** Pivotal trials that were comparative or single-arm
- **Patient populations**:
  - Mild-to-moderate open-angle glaucoma according to the Hodapp-Parrish-Anderson criteria on visual field defect
  - Refractory glaucoma where IOP is uncontrolled by all previous treatments
  - **Type of MIGS by approaches to fluid drainage**: (1) Trabecular bypass stent with and without cataract surgery (TB+C, TB) for mild-to-moderate glaucoma; (2) suprachoroidal stent with cataract surgery (S+C) for mild-to-moderate glaucoma; and (3) subconjunctival stent with and without cataract surgery (SC+C, SC) for refractory glaucoma. In terms of sequencing of these stents, the SC stent is typically for end-stage glaucoma, and therefore, implanted when IOP is uncontrolled on TB or S type of stents.
- **Trial characteristics and outcomes reviewed**:
  - Study design – type of trial, interventions, sample size, follow-up duration, geographical location
  - Baseline characteristics – age, treatment naïve, mean medication use, IOP with and without washout
  - Outcomes – percentage of patients with hypotony (<6 mmHg), controlled (6-21 mmHg) and uncontrolled (>21 mmHg) IOP, and AEs

Economic Analysis

- **Time horizon**: 1 year
- **Data source**:
  - The risk of AEs and efficacy in terms of hypotony, controlled and uncontrolled IOP at 12 months were obtained from trials. Only AEs impacting the hospital budget were considered. When efficacy was not reported, a lognormal distribution using the mean and standard deviation of IOP at 12 months was used to estimate the proportion of patients with hypotony, controlled versus uncontrolled IOP.
  - Resource utilization for surgery, AEs, and ophthalmology visits were obtained via expert opinion.
  - Unit costs of ophthalmologist visits, AE-related procedures and surgeries were obtained from the Spanish medical cost database Oblikue [6], and pharmacy costs (mitomycin) from the Spanish college of Pharmaceutics database Bot Plus Web [7].
  - MIGS price was from the Valencia regional purchasing agency [8].
- **Adjustments to unit costs:** Costs were inflated to 2017 using consumer price index from the National Statistics Institute [3].
- **Analyses:** Base case, 1-way sensitivity analyses and probabilistic sensitivity analyses.

RESULTS

Clinical Review

- In patients with a need of concurrent cataract surgery, direct comparison between TB + C and S + C was not feasible due to differences in the method of IOP measurement at follow-up. The pivotal trial for TB + C measured medicated IOP, which is a real-world scenario whereas the trial for S + C measured unmedicated IOP.
- The baseline mean medication use was 33.3-94.4% times higher in the refractory population compared with the mild-to-moderate patients.
- Baseline utilization of medications varied by the type of MIGS in patients with mild-to-moderate glaucoma: 100% of patients in the TB + C and TB groups consumed medications at baseline compared with 83.2% in the S + C group.

RESULTS

Clinical Review (continued)

- Differences were observed in the baseline average visual field defect mean deviation scores between the two populations: -3.77, -5.20, -3.37, and -15 dB in the TB + C, TB, S + C and SC + C groups, respectively. Baseline VF defect has not been reported in the SC group.
- >50% of patients in all treatment groups had IOP under control at 12 months (Table 1).
- Reduction in IOP by ≥20% was observed in 66%, 90.2%, 82%, and 55.6% of unmedicated patients in the TB + C, TB, S + C and SC groups, respectively. An estimated 76.3% of patients in the SC + C group experienced ≥20% reduction in IOP while consuming some or fewer medications compared to baseline. Reduction in mean medication use at 12 months was 1.4, 1.6, 1.2, 1.8, and 1.9, respectively.
- No patients in the standalone TB group had uncontrolled IOP (>21 mmHg) or experienced an AE with a cost consequence for hospitals at 12 months (Table 1).
- 24.6% of patients implanted with SC experienced hypotony (Table 1).

Table 1: Efficacy and safety outcomes of MIGS at 12 months

Type of Outcome	Variable	Mild-to-moderate glaucoma [9-12]			Refractory glaucoma [13,14]	
		TB + C (N=116)	TB* (N=41)	S + C** (N=374)	SC + C (N=65)	SC (N=111)
Efficacy	Hypotony, %	1.0	0.0	6.1	24.6	24.6
	Controlled IOP, %	67.0	100.0	70.0	52.5	69.1
	Uncontrolled IOP, %	32.0	0.0	23.9	22.9	6.3
Adverse Events	Needling with mitomycin, %	0.0	0.0	0.0	32.3	Assumed similar to SC + C treatment, except for posterior capsular opacification (0%)
	Hypotony, %	1.0	0.0	6.1	24.6	
	Anterior chamber shallowing, %	0.0	0.0	3.0	1.5	
	Cyclodialysis cleft, %	0.0	0.0	1.0	0.0	
	Peripheral anterior synechiae, %	0.0	0.0	6.7	1.5	
	Stent obstruction, %	4.0	0.0	3.6	0.0	
	Dislodgement of stent/movement/repositioning, %	3.0	0.0	1.4	1.5	
	Explant of stent, %	0.0	0.0	0.2	10.7	
	Anterior chamber tap, %	0.0	0.0	0.0	9.2	
	Choroidal effusion/detachment, %	0.0	0.0	0.0	3.1	
	Posterior capsular opacification, %	6.0	0.0	0.0	4.6	
	Would/bleb leak, %	0.0	0.0	0.0	9.2	

* Katz et al. compared the efficacy of 1 vs. 2 vs. 3 standalone TBs. Outcome for 2 standalone TBs is presented above. Only unmedicated IOP results were available for S + C. Efficacies for TB + C, TB, SC + C and SC were based on medicated IOP, which reflects a real-world setting.
** The trial reported the rate of AEs at 24 months. The data shown above is for 12 months.
Note: The definition of controlled IOP in patients implanted with CyPass was 6-18 mmHg. Uncertainty in estimates due to variation in definition was tested in 1-way sensitivity analyses. The percentage of patients with uncontrolled IOP was varied between 19.6% to 28.5% for CyPass.

Economic Analysis

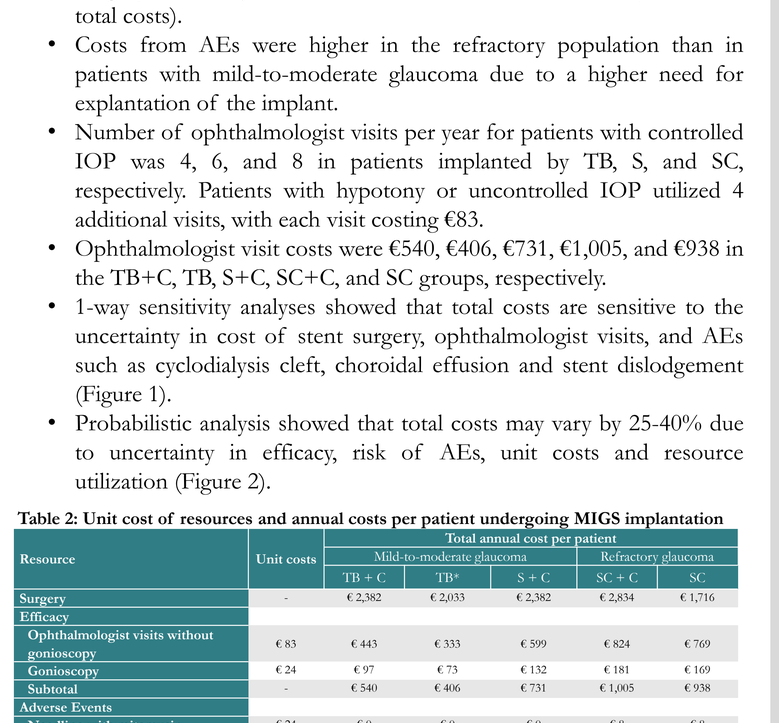
- Annual costs for TB+C, TB, S+C, SC+C and SC were €2,983, €2,439, €3,189, €4,077 and €2,886, respectively (Table 2).
- Surgery was a major driver of total costs across all MIGS (59-83% of total costs).
- Costs from AEs were higher in the refractory population than in patients with mild-to-moderate glaucoma due to a higher need for explantation of the implant.
- Number of ophthalmologist visits per year for patients with controlled IOP was 4, 6, and 8 in patients implanted by TB, S, and SC, respectively. Patients with hypotony or uncontrolled IOP utilized 4 additional visits, with each visit costing €83.
- Ophthalmologist visit costs were €540, €406, €731, €1,005, and €938 in the TB+C, TB, S+C, SC+C, and SC groups, respectively.
- 1-way sensitivity analyses showed that total costs are sensitive to the uncertainty in cost of stent surgery, ophthalmologist visits, and AEs such as cyclodialysis cleft, choroidal effusion and stent dislodgement (Figure 1).
- Probabilistic analysis showed that total costs may vary by 25-40% due to uncertainty in efficacy, risk of AEs, unit costs and resource utilization (Figure 2).

Table 2: Unit cost of resources and annual costs per patient undergoing MIGS implantation

Resource	Unit costs	Total annual cost per patient				
		Mild-to-moderate glaucoma			Refractory glaucoma	
		TB + C	TB*	S + C	SC + C	SC
Surgery	-	€ 2,382	€ 2,033	€ 2,382	€ 2,834	€ 1,716
Efficacy						
Ophthalmologist visits without gonioscopy	€ 83	€ 443	€ 333	€ 599	€ 824	€ 769
Gonioscopy	€ 24	€ 97	€ 73	€ 132	€ 181	€ 169
Subtotal	-	€ 540	€ 406	€ 731	€ 1,005	€ 938
Adverse Events						
Needling with mitomycin	€ 24	€ 0	€ 0	€ 0	€ 8	€ 8
Hypotony	€ 27	€ 0	€ 0	€ 2	€ 7	€ 7
Anterior chamber shallowing	€ 66	€ 0	€ 0	€ 2	€ 1	€ 1
Cyclodialysis cleft	€ 1,128	€ 0	€ 0	€ 11	€ 0	€ 0
Peripheral anterior synechiae	€ 433	€ 0	€ 0	€ 29	€ 7	€ 7
Stent obstruction	€ 433	€ 17	€ 0	€ 16	€ 0	€ 0
Dislodgement/movement/repositioning	€ 1,176	€ 35	€ 0	€ 16	€ 18	€ 18
Explant	€ 1,176	€ 0	€ 0	€ 2	€ 126	€ 126
Anterior chamber tap	€ 148	€ 0	€ 0	€ 0	€ 14	€ 14
Choroidal effusion	€ 2,616	€ 0	€ 0	€ 0	€ 41	€ 41
Posterior capsular opacification	€ 139	€ 8	€ 0	€ 0	€ 6	€ 0
Bleb leak	€ 148	€ 0	€ 0	€ 0	€ 12	€ 12
Subtotal	-	€ 61	€ 0	€ 77	€ 238	€ 232
Total	-	€ 2,983	€ 2,439	€ 3,189	€ 4,077	€ 2,886

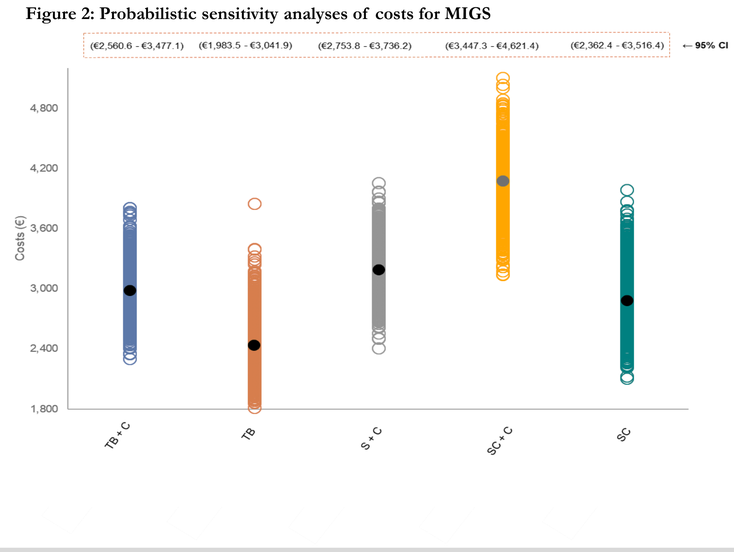
* Results are for the implantation of 2 TB MIGS

Figure 1: Tornado charts for one-way sensitivity analysis of costs for MIGS



RESULTS

Figure 2: Probabilistic sensitivity analyses of costs for MIGS



LIMITATIONS

- Ophthalmologists may have become more skilled at implanting the stents since the publication of the pivotal trials, and therefore, costs may be overestimated.
- Most trials were conducted outside of Spain. Differences in glaucoma treatment practice and access to treatments between countries may impact the cost estimates for Spain.
- The impact of MIGS on the use of medications was not included in the analysis.
- The cost and availability of MIGS varies between regions in Spain. Given that the objective of the study was to estimate the cost of MIGS in Spain, we varied the cost by ±25% to accommodate possible variation in cost between regions in the sensitivity analyses.

DISCUSSION

- Both mild-to-moderate and refractory glaucoma patients experienced a reduction in IOP and medication use over 12 months, regardless of the type of MIGS.
- The efficacy and safety of SC stent procedure has been examined in patients with severe glaucoma who failed all previous treatment modalities as opposed to TB and S stents surgeries that have shown to reduce IOP in the mild-to-moderate glaucoma population.
- According to the National Institute for Health and Care Excellence (Interventional procedures guidance 575; February 2017), the evidence for the use of TB stent is adequate in quality and quantity. No major safety concerns have been raised for the TB stent. Other stents such as SC are currently undergoing review by NICE.
- Significant differences exist between the trials in the mild-to-moderate population that prevents meaningful comparative inferences.

CONCLUSION

- In the mild-to-moderate population, follow-up visits required for the surveillance of AEs such as hypotony was a key driver of differences in annual treatment cost between TB and S type of stents.
- In the refractory population, annual treatment costs were higher in the SC+C group compared to the SC group, in part due to the cost of cataract surgery, ophthalmologist visits, and AEs.
- When considering costs of MIGS, one must consider the population of interest, whether cataract surgery is performed, subsequent ophthalmologist visits, and the risk of AEs, in addition to the price of stents.

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