SURGICAL PEARLS
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Will the Cost of Clinical Trials Quash Change in Glaucoma Treatment?

Financial burden compromises phase 3 trials and prolongs the approval of surgical devices.

BY ALAN L. ROBIN, MD

Increased public awareness and newer technology have improved clinicians' ability to detect glaucoma at earlier stages in the disease process. It is widely believed that, the earlier the disease is detected, the more successful treatment can be. Regrettably, there are no attractive therapies to offer to patients with early-stage glaucoma. In cataract surgery, a 98% successful therapy requiring few follow-up visits provides rapid and satisfactory improvement for a noticeable symptom. In contrast, glaucoma is largely asymptomatic, and the treatment options are prolonged and most often have noticeable side effects. The result is negative social marketing among peers, which ultimately negates any positive effect from early detection and is partially why individuals do not refill prescriptions and are not adherent.

INITIAL OPTIONS FOR TREATMENT

Initially, most glaucoma patients receive a prescription for topical ocular hypotensive medications, which are known to effectively minimize the risk of damage to the optic nerve when used according to the prescribed regimen.[1] These drugs have been associated with blurred vision, stinging, foreign body sensation, and even cardiovascular or pulmonary adverse events.[2-4] The physical side effects likely combine with other factors related to cost and convenience to result in dismal adherence rates. In the Glaucoma Adherence and Persistency Study (GAPS), only 10% of subjects were 100% compliant with filling their prescriptions over a 12-month period.[5] Moreover, Stone and colleagues demonstrated that, even when patients fill their prescriptions, only 21.9% instill a single drop without touching the surface of the eye.[6] Additionally, recent studies suggest that patients who have less severe disease or who recently started taking medications are among the least likely to be adherent.[7,8]

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The efficacy of selective laser trabeculoplasty is considered to be similar to that of topical medications for initial glaucoma therapy.[9] Topical therapy does not work for all patients, and the success rate drops over time. Likewise, the effect of laser trabeculoplasty diminishes significantly with time in a lifelong disease. The Collaborative Initial Glaucoma Treatment Study (CIGITS) compared medical therapy to filtration surgery in newly diagnosed glaucoma patients.[10] Although both modalities were comparably adept at preventing disease progression, surgery is associated with complications such as failure, cataract, endophthalmitis, hypotony, and a long-term risk of bleb-related infections. Newer surgical options involving intraoperative gonioscopy have been difficult to perform or have insufficiently lowered IOP. None of the new surgeries is approved in eyes not requiring cataract surgery.

NONPENETRATING GLAUCOMA SURGERY

CO_2 laser-assisted sclerectomy surgery (CLASS) is a relatively new procedure that has the potential to fulfill an unmet need in the glaucoma space. The surgeon creates a superficial scleral flap via a peritomy and then

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uses a CO_2 laser (IOPtimate System; IOPtima) to ablate the scleral tissue directly above Schlemm canal. The ablation ceases once aqueous humor begins to percolate through the thinned membrane. The scleral flap is then replaced and sutured.

In a study of 37 patients with primary and pseudoexfoliative open-angle glaucoma who underwent CLASS, the mean baseline IOP dropped from 26.3 ±7.8 to 14.4 ±3.4 mm Hg 6 months postoperatively, a reduction sustained through 12 months.[11] Because the globe was not penetrated, intra- and postoperative complications were mild and transitory.

APPROVAL CHALLENGES

Unfortunately, like many small companies, IOPtima is caught in a regulatory quagmire. Whereas CE Mark approval was relatively easy to obtain in Europe, the same has not been true of FDA approval. Although extensive testing requirements are for the benefit and protection of all, increased regulation and possibly excessively risk-averse interpretations of those regulations are just two factors complicating the FDA approval process. The financial burden of producing phase 3 data might be eliminating superior surgical options for glaucoma therapy before their worth can be proven.

In the United States, the manufacturers of medical devices and pharmaceuticals face a rising cost of clinical trials. In 2005, the research and development cost of a new drug was $1.3 billion,[12] and costs are calculated to increase 7.4% annually over inflation.[13] Because scarce investment dollars are much more likely to go to drugs than devices, fewer new technologies and procedures can come to market.

Several studies have been conducted on the CLASS procedure. Overall, the data have shown that the procedure is relatively easy to learn, have supported its safety, and demonstrated that it substantially lowers IOP. Further research is needed. The studies have not been controlled, and they do not directly compare the safety and efficacy of CLASS to trabeculectomy, the gold standard. Additionally, long-term follow-up is absent in many studies. According to the company, a long-term follow-up study of a substantially large cohort without a trabeculectomy control is planned for publication.

CLASS is already approved in Europe, China, Mexico, India, and Israel, and more than 700 patients have received the treatment. For US patients to undergo the procedure, IOPtima will have to overcome the hurdles posed by the FDA approval process. ■

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