CrossMark

American Academy of Ophthalmology
The Eye M.D. Association

A Randomized Trial of a Schlemm's Canal Microstent with Phacoemulsification for Reducing Intraocular Pressure in Open-Angle Glaucoma

Norbert Pfeiffer, MD, PhD,[1] *Julian Garcia-Feijoo, MD, PhD,*[2] *Jose M. Martinez-de-la-Casa, MD, PhD,*[2] *Jose M. Larrosa, MD, PhD,*[3] *Antonio Fea, MD, PhD,*[4] *Hans Lemij, MD, PhD,*[5] *Stefano Gandolfi, MD, PhD,*[6] *Oliver Schwenn, MD,*[7] *Katrin Lorenz, MD,*[1] *Thomas W. Samuelson, MD*[8]

Purpose: To assess the safety and effectiveness of the Hydrus Microstent (Ivantis, Inc, Irvine, CA) with concurrent cataract surgery (CS) for reducing intraocular pressure (IOP) in open-angle glaucoma (OAG).

Design: Prospective, multicenter, randomized, single-masked, controlled clinical trial.

Participants: One hundred eyes from 100 patients 21 to 80 years of age with OAG and cataract with IOP of 24 mmHg or less with 4 or fewer hypotensive medications and a washed-out diurnal IOP (DIOP) of 21 to 36 mmHg.

Methods: On the day of surgery, patients were randomized 1:1 to undergo CS with the microstent or CS alone. Postoperative follow-up was at 1 day, 1 week, and 1, 3, 6, 12, 18, and 24 months. Washout of hypotensive medications was repeated at 12 and 24 months.

Main Outcome Measures: Response to treatment was defined as a 20% or more decrease in washed out DIOP at 12 and 24 months of follow-up compared with baseline. Mean DIOP at 12 and 24 months, the proportion of subjects requiring medications at follow-up, and the mean number of medications were analyzed. Safety measures included change in visual acuity, slit-lamp observations, and adverse events.

Results: The proportion of patients with a 20% reduction in washed out DIOP was significantly higher in the Hydrus plus CS group at 24 months compared with the CS group (80% vs. 46%; $P = 0.0008$). Washed out mean DIOP in the Hydrus plus CS group was significantly lower at 24 months compared with the CS group (16.9±3.3 mmHg vs. 19.2±4.7 mmHg; $P = 0.0093$), and the proportion of patients using no hypotensive medications was significantly higher at 24 months in the Hydrus plus CS group (73% vs. 38%; $P = 0.0008$). There were no differences in follow-up visual acuity between groups. The only notable device-related adverse event was focal peripheral anterior synechiae (1−2 mm in length). Otherwise, adverse event frequency was similar in the 2 groups.

Conclusions: Intraocular pressure was clinically and statistically significantly lower at 2 years in the Hydrus plus CS group compared with the CS alone group, with no differences in safety. *Ophthalmology 2015;122:1283-1293 © 2015 by the American Academy of Ophthalmology.*

See Editorial on page 1277.

Glaucoma remains the second leading cause of blindness worldwide.[1] Elevated intraocular pressure (IOP) is an important risk factor for the progression of the disease. It can be lowered medically or surgically depending on severity and progression.[2,3] Control of IOP has been shown to reduce glaucoma progression and the resultant visual field loss.[4,5] Topical medications have a proven record of efficacy and safety, but they are accompanied by side effects such as exacerbation of dry eye and ocular surface disease[6] and present clinical limitations related to compliance and adherence.[7–9] Furthermore, chronic medication use may reduce the success rate of subsequent glaucoma filtration surgery.[10]

A new class of microinvasive glaucoma surgery (MIGS) devices[11] has been developed that do not require scleral incisions and increase outflow by directly accessing Schlemm's canal[12] or by shunting fluid from the anterior chamber to the suprachoroidal[13] or subconjunctival[14] space. Because MIGS devices are placed ab interno using the same clear corneal incision created for phacoemulsification, they are readily combined with cataract surgery (CS). Microinvasive glaucoma surgery approaches could avoid complications of traditional glaucoma surgery,[15] such as hypotony and bleb revision, and may provide an option for treatment of mild as well as more advanced disease.

The purpose of the HYDRUS II study was to evaluate clinically a new Schlemm's canal scaffold (Hydrus Microstent; Ivantis, Inc, Irvine, CA) for IOP reduction after concomitant CS. The Hydrus Microstent is an 8-mm long crescent-shaped open structure, curved to match the shape of Schlemm's canal. The microstent is implanted ab interno

http://dx.doi.org/10.1016/j.ophtha.2015.03.031
ISSN 0161-6420/15

through a clear corneal incision into Schlemm's canal using a preloaded hand-held injector. After being implanted, the microstent bypasses the trabecular meshwork and dilates Schlemm's canal over 3 clock hours to provide direct aqueous access from the anterior chamber to multiple collector channels (Fig 1) without interfering with or damaging the structures.[16]

Methods

Study Design

The HYDRUS II study was a prospective, single-masked, randomized, controlled clinical trial conducted at 7 European investigational sites (see listing of authors institutional affiliations). The study protocol was approved by the medical ethics committee at each site and conducted according the principals described in the Declaration of Helsinki. All study subjects provided written informed consent before commencing participation in the trial. Patients from the participating centers with concurrent open-angle glaucoma and cataract who met the study entry criteria were assigned randomly in a 1:1 ratio according to a computer-generated listing just before surgery to undergo either CS (phacoemulsification and intraocular lens [IOL] implantation) with the Hydrus Microstent (Hydrus plus CS group) or CS alone (CS group). Subjects were followed up for 2 years, at which time the efficacy and safety end points were ascertained. Subjects remained masked to treatment assignment for the course of the study.

The study was designed by the first and last authors and the sponsor (Ivantis, Inc) in accordance with the study design recommendations described in the American National Standards Institute guidance for glaucoma aqueous shunts.[17] The study was registered in the National Library of Medicine database (clinicaltrials.gov identifier, NCT01818115). The data were 100% source document verified by independent monitors (MediTech Strategic Consultants BV, Vaals, The Netherlands) with funding provided by the sponsor. The analyses were conducted by the sponsor.

Study Patients

Patients with concurrent cataract and open-angle glaucoma were enrolled prospectively in the study. Only 1 eye per patient was eligible for treatment, although both eyes could be screened for inclusion. The study eye was required to have an IOP of 24 mmHg or less with no more than 4 hypotensive medications, Shaffer grade III or IV chamber angle in all quadrants, and Humphrey (Carl Zeiss, Jena, Germany) visual field changes characteristic of glaucoma or glaucomatous optic nerve damage confirmed by ophthalmoscopy and nerve fiber layer imaging. Glaucoma severity was limited to subjects considered capable of safely undergoing medication washout. Before surgery, subjects were washed out of all hypotensive medications in the study eye for a variable period, depending on the class of medication in use at the time of screening. The washout protocol is described in the Ocular Hypertension Treatment Study.[18] At the completion of the washout, a preoperative baseline diurnal IOP (DIOP) value was obtained by averaging 3 Goldmann tonometry measurements obtained 4 hours apart between 8AM and 4PM. The tonometry protocol used a 2-person system (an observer and a reader), and 2 readings were obtained at each time point during the day. If the difference in the 2 measurements was more than 2 mmHg, a third measurement was obtained. The average of 2 measurements or the median value of 3 was used for the time point, and the average of the IOP measurements at all 3 time points was the mean DIOP. The DIOP value was required to be between 21 and 36 mmHg for study inclusion. Clinical exclusion criteria included angle-closure glaucoma, secondary glaucomas except pseudoexfoliation or pigment dispersion syndromes, exudative age-related macular degeneration (AMD), proliferative diabetic retinopathy, or significant risk of glaucomatous vision loss because of washout of IOP-lowering medications. Anatomic exclusion criteria were narrow angle or other angle abnormality visible on gonioscopy, central corneal thickness of less than 480 μm or more than 620 μm, or clinically significant corneal dystrophy. Patients with prior corneal surgery, argon laser trabeculoplasty, cycloablation, or any incisional glaucoma procedure, such as trabeculectomy, tube shunts, deep sclerectomy, or canaloplasty, also were excluded.

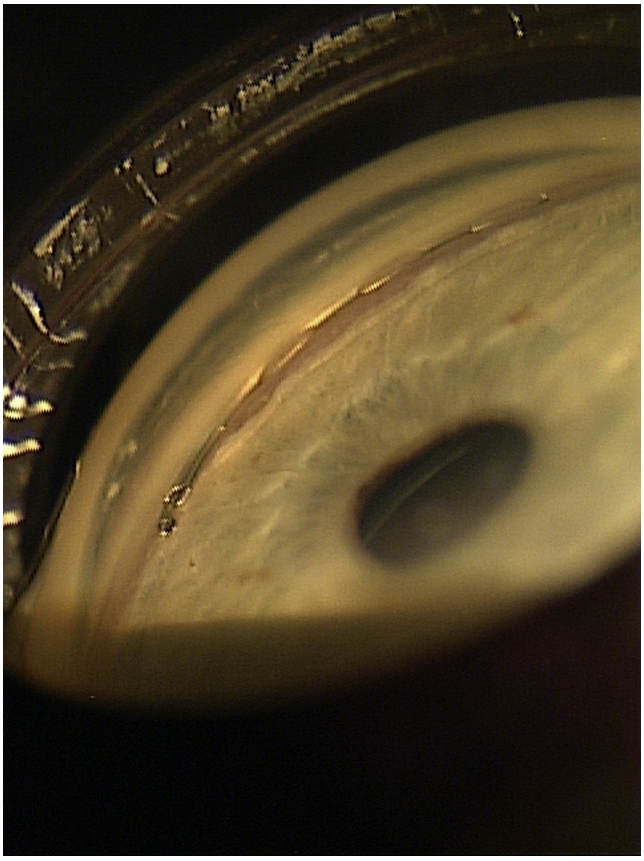

Figure 1. The Hydrus Microstent (Ivantis, Inc, Irvine, CA) is 8 mm in length. The 7-mm scaffold segment resides within the lumen of Schlemm's canal, and the 1-mm inlet portion resides within the anterior chamber. The microstent is designed to fit the curvature of the canal without obstructing collector channel ostia located along the posterior wall. (Photograph courtesy Jason Jones, MD.)

Study Device

The microstent is made from nitinol (nickel–titanium alloy), a material with unique shape memory properties that has been used widely in vascular and other medical applications.[19–21] The biocompatibility of nitinol for ocular applications has been reported previously,[22] and the Hydrus Microstent has been evaluated in rabbit and primate ocular models.[23] Multiple laboratory studies examining the Hydrus Microstent using human cadaveric tissue in an anterior segment perfusion model have demonstrated an increase in outflow facility compared with untreated controls.[24,25]