

Dexamethasone Implant for DME

The Posurdex device has shown safety and efficacy in phase 2 and 2b studies to date.

BY BARUCH D. KUPPERMANN, MD, PhD

Diabetic macular edema (DME) is the most common cause of visual acuity loss in patients with diabetic retinopathy.¹ The mainstay of treatment for DME remains focal/grid photocoagulation,² but there has been increasing interest in the feasibility of treating the disease using sustained delivery of low-dose corticosteroids.

The Posurdex Sustained Dexamethasone Drug Delivery System (Allergan) is a biodegradable implant in which the drug is incorporated into a polymer matrix. As the polymer breaks down into inert compounds over time, the drug is released (Figure 1).

An extruded form of the implant, used in phase 2b and 3 clinical trials, is implanted with a 22-gauge applicator through a self-sealing wound in the pars plana. This can be done as an office-based procedure, without a trip to the operating room. The implant does not have to be sutured into place.

PHASE 2 TRIAL

A phase 2 dose-ranging clinical trial evaluated a surgi-

cally inserted version of the Posurdex implant.³ The device was implanted through a 20-gauge pars plana incision in the operating room, and the sclerotomy and overlying conjunctiva were sutured.

The purpose of the trial was to evaluate the safety and efficacy of dexamethasone in this novel drug delivery system for the treatment of persistent macular edema. The trial included patients with DME and diagnoses other than DME. In the 315 patients enrolled, the diagnosed cause of macular edema was Irvine-Gass syndrome in 8.6%, uveitis in 4.4%, retinal vein occlusion in 32.7%, and DME in the largest percentage of patients, 54.3%.

In this randomized, multicenter, controlled, parallel group, dose-ranging study, one eye per patient was selected as the study eye and randomly assigned to observation, 350 µg Posurdex, or 700 µg Posurdex. Patients had macular edema that persisted more than 90 days after standard of care laser or medical therapy with a best corrected visual acuity (BCVA) of 20/40 or worse, but no worse than 20/200.

In these patients with persistent macular edema, with

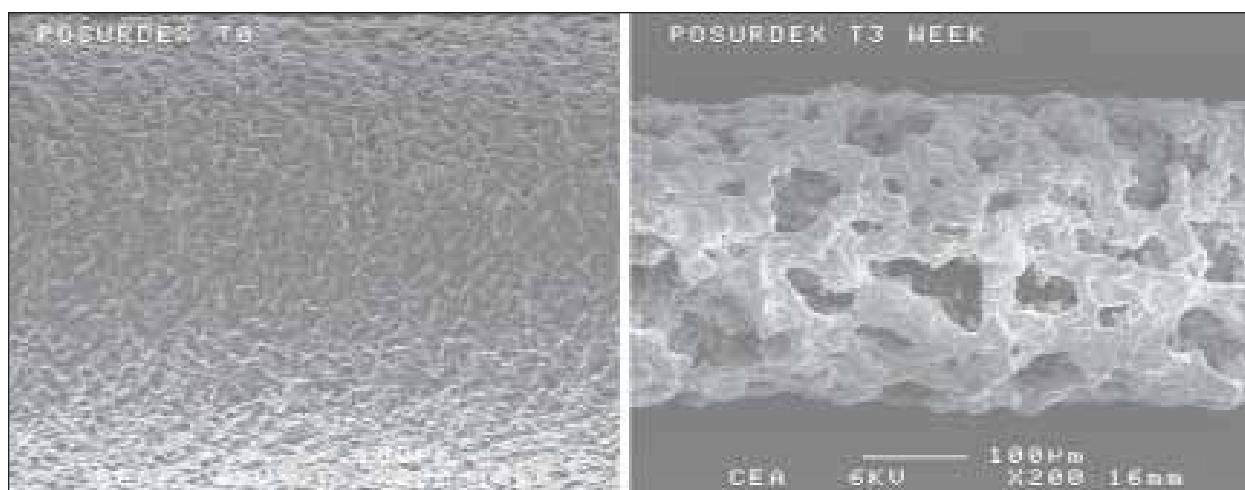


Figure 1. As the polymer breaks down into inert compounds over time, the drug is released.

eyes that had failed prior therapy, 18% of eyes had a three-line improvement in BCVA at 90 and 180 days with the 700 µg implant vs 6% of observed patients ($P=.006$). The authors concluded that the 700 µg dexamethasone implant produced clinically and statistically significant improvements in visual acuity that were apparent by day 60 and persistent through day 180. Significant improvements were also seen in retinal thickness and fluorescein leakage.

Most adverse events were mild and occurred during the first week after surgery. Increases in intraocular pressure (IOP) were managed by observation or with topical IOP-lowering medication. There was no increase in cataracts and no treatment-related endophthalmitis.

When the investigators looked at the subgroup of 171 patients with DME, they found that the data were consistent with those for the overall patient population. There was a statistically significant benefit for the 700 µg implant over observation at day 90 for the primary outcome of BCVA improvement. It must be noted, however, that the study was not powered to evaluate statistically significant differences between treatment and observation groups in this subset.

No patient in the 700 µg group in the DME subgroup needed rescue therapy with intravitreal triamcinolone acetonide or laser between 3 months and 6 months, while two in the 350 µg group and four in the observation group needed rescue.

Clinically significant improvements in visual acuity in patients with DME persisted at least through month 6, and they were accompanied by improvements in macular thickness and fluorescein leakage, the authors concluded. As with the overall patient population, most adverse events were mild, and increases in IOP were controlled with observation or with IOP-lowering medications.

PHASE 2B TRIAL

A phase 2b clinical trial evaluated the safety and performance of an applicator for placement of the extruded form of Posurdex.⁴ The trial also compared the safety of applicator placement versus incisional placement of the device.

In this prospective, multicenter trial, all patients underwent insertion of the 700 µg dose of Posurdex through the pars plana. They were randomly assigned, 2:1, to applicator or incisional placement. The extruded form of the device was used in applicator placement, and the tableted form—the form used in the phase 2 trial described above—was used for surgical placement.

Of 30 patients enrolled, 19 received the applicator-inserted extruded Posurdex and 10 received the surgically implanted version. (One patient was enrolled but

declined to be treated.) At 6 months, visual acuity results are similar to those in the phase 2 trial; in both groups, 20% of patients had a three-line or greater improvement in BCVA.

The rate of all ocular adverse events was less in the applicator group than in the incisional group. There were no cases of endophthalmitis or retinal detachment in either group. There was one case of nuclear cataract in each treatment group. There was no difference in the number of reports of elevated IOP (increase greater than 10 mm Hg) in either group (three patients in the incisional group, two patients in the applicator group).

CONCLUSIONS

In patients with persistent DME, a single Posurdex dexamethasone implant treatment produced statistically significant BCVA improvements 90 days after treatment and was well tolerated for 180 days in the phase 2 study. The phase 2b study evaluating the sutureless applicator placement of the device showed safety equal to or better than incisional placement and equal efficacy for both approaches to placement.

The 700 µg Posurdex insert may have potential as a treatment for persistent macular edema. Results of a phase 3 study of the device in patients with DME has completed enrollment and is in follow-up phase. A phase 3 study of the device in patients with macular edema due to retinal vein occlusion is complete, and results are expected to be announced later this year. ■

Baruch D. Kuppermann, MD, PhD, is a Professor and Chief of the Retina Service at the Gavin Herbert Eye Institute in the Department of Ophthalmology at the University of California, Irvine. Dr. Kuppermann is a member of the Retina Today editorial board. He reports that he receives clinical research grants from Alimera, Allergan, Inc., Genentech, Inc., Regeneron, Inc., and Thrombogenics; he is a consultant to Allergan, Inc., B Braun, CoMentis, Fovea, Genentech, Inc., Glaukos, Novartis, Ophthotech, Pfizer, ScyFix, Surmodics, TargeGen, and Vitreoretinal Technologies, Inc.; he is a member of the data and safety monitoring board for Neovista, and is a medical monitor for Novagali. Dr. Kupperman may be reached at bdkupper@uci.edu.



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