MODULE 10.8
Clinical Studies and Treatment Data - PLACID

PLACID[1]

Study Name	Dexamethasone Intravitreal Implant in Combination With Laser Photocoagulation for the Treatment of Diffuse Diabetic Macular Edema
Purpose of study	To determine if the combination of Ozurdex and laser is more effective than laser alone in diffuse diabetic macular edema (DME)
Study authors	Callahan DG, Gupta S, Boyer DS, Ciulla TA, Singer MA, Kuppermann BD, Liu C-C, Li X-Y, Hollander DA, Schiffman RM, Whitcup SM for the Ozurdex PLACID Study Group
Published in	*Ophthalmology.* 2013;120:1843-1851.
Study also known as	PLACID
Subsequent studies	N/A

Study Overview

PLACID enrolled 253 patients at 48 centers in the US and Canada who had retinal thickening and impaired vision from diffuse DME.[1] This randomized, controlled, multicenter, double-masked, parallel study evaluated if the combination of dexamethasone 0.7 mg with laser photocoagulation therapy 1 month after implantation was more effective than laser photocoagulation therapy alone. The primary outcome was the percentage of patients with at least 10 Early Treatment Diabetic Retinopathy Study (ETDRS) letter improvements from baseline at 1 year.

Eyes included in this study had to have a mean retinal thickness of at least 275 µm in the 1-mm central macular subfield due to diffuse DME not amenable to laser, as determined by optical coherence tomography (OCT). Further, inclusion criteria mandates diffuse macular capillary bed leakage evident on fluorescein angiography (FA), and a best-corrected visual acuity (BCVA) between 34 and 70 ETDRS letter (about 20/40 to 20/200). Exclusion criteria included uncontrolled systemic disease, use of systemic corticosteroids within 12 weeks before study enrollment, active ocular infection, glaucoma, or a history of intraocular pressure (IOP) - spike steroid response.

At each of the follow-up visits through month 9, the differences between treatment groups were statistically significant, with greater improvement in BCVA in eyes treated with dexamethasone implant plus laser than in eyes treated with laser alone ($P \leq .013$)[1] (see Figure 1). The percentage of patients who gained 10 letters or more did not differ between the treatment groups at month 12 (although there were statistically significant differences at months 1 and 9 in favor of the combination group). Decreases in the area of diffuse vascular leakage as measured angiographically were significantly larger in the combined group through month 121 (see Figure 2).

Study Implications

Diffuse DME is difficult to treat with laser alone.[1] This is one of the few studies to evaluate this type of DME using an intravitreal corticosteroid and photocoagulation therapy.

The study authors found that the combined treatment improved outcomes, and by month 4 patients in the combined group were about twice as likely to gain 10 or more ETDRS letters than those treated with laser alone. Although both groups had reduced edema, the differences in edema reduction were not statistically significant between the two groups by month 12. However, only the combination group had the added benefit of improved vision.[1]

As with other corticosteroid studies, there was a high risk of cataract formation in phakic patients, and the combination group also had increased IOP at much higher rates than the laser-only group.

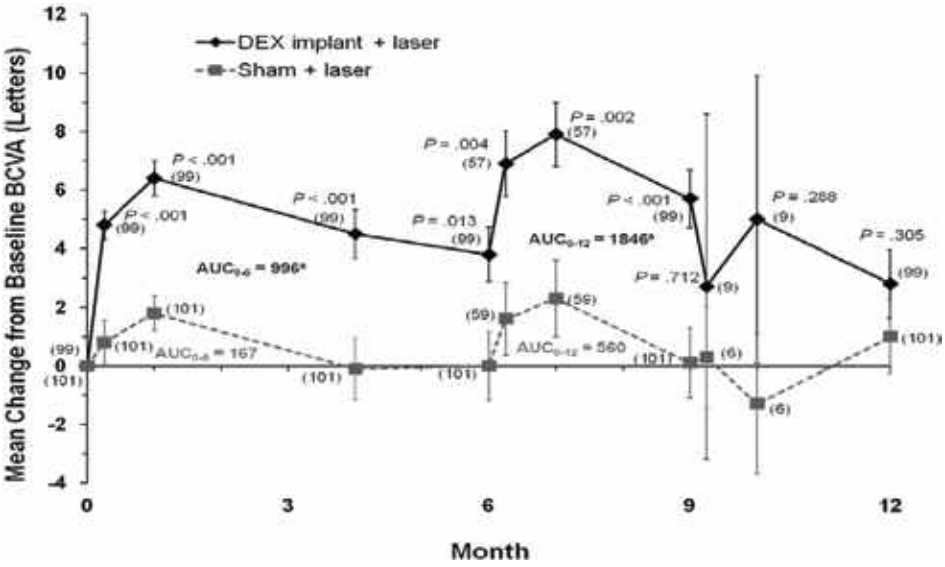

Figure 1: Mean change from baseline in BCVA.

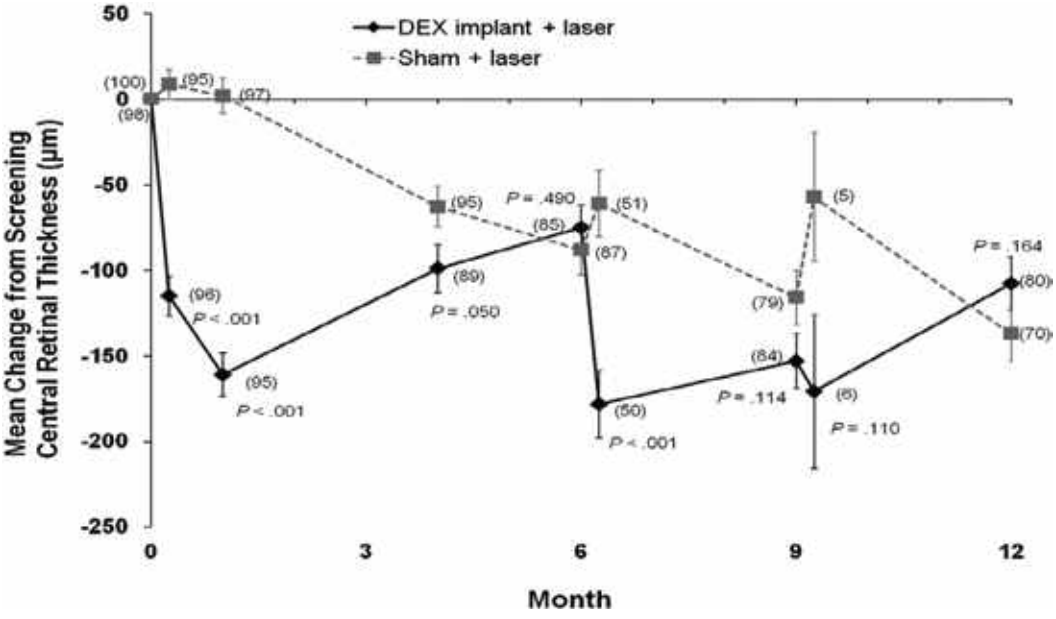

Figure 2: Mean change in central retinal subfield thickness.

Also, in this group of patients, the vision gain equated to less than 1 line of vision. Although treatment burden with this implant is certainly less than with anti-VEGF drugs, the vision gains are not necessarily enough to warrant making this therapy a first-line treatment.

Take-Home Points

- Dexamethasone implant in combination with laser therapy improved both edema and vision in patients with diffuse DME, a traditionally difficult-to-treat group.
- The side effects of IOP elevation, cataract formation in phakic patients, and less BCVA gain with this drug than anti-VEGF drugs, makes this drug a second-line treatment for most patients.

References

1. Callanan DG, Gupta S, Boyer DS, et al. Dexamethasone intravitreal implant in combination with laser Photocoagulation for the treatment of diffuse diabetic macular edema. *Ophthalmology*. 2013;120:1843-1851.