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Direttore : S. Cillino

Edema Maculare Diabetico: opzioni terapeutiche

A.M. Sabella, G.Scianna, S. Piscitello, M.Vadala', S. Cillino

Campofelice di Roccella
14-16 Aprile 2016

SOSi
Società Oftalmologica Siciliana

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Opzioni di trattamento

- Laser
- Farmaci Steroidei
- Farmaci anti-VEGF

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Nostra esperienza

16 pazienti con EMD trattati con impianto iv di Desametasone (OZURDEX), follow-up min 12 mesi:

- 4 pz vitrectomizzati (5 occhi)
- 8 pz pseudofachici (8 occhi)
- Tutti pz non Naive

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Nostra esperienza

Valutazioni:

- TMV (total macular volume)
- Visus
- Pz pseudofachici vs fachici
- Pz vitrectomizzati
- Aumento della IOP

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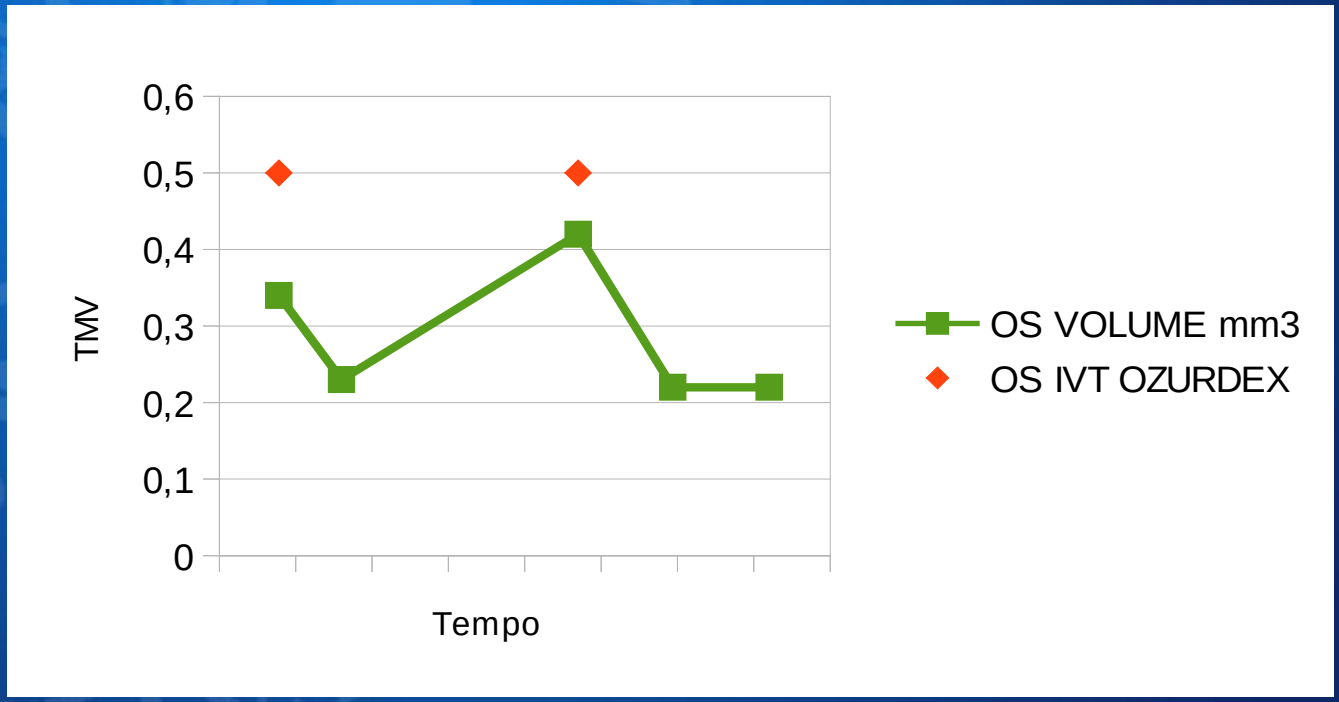
Valutazioni

Volume Maculare Totale(mm3) TMV

Netta riduzione del TMV in tutti i pz trattati con Dex.



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Valutazioni

Numero di iniezioni

- numero medio di iniezioni per paziente: 1.1
- intervallo medio prima di iniettare nuovamente Ozurdex®: 5.5 mesi

réalités OPHTALMOLOGIQUES # 213_May 2014

GENERAL REVIEWS

MOZART Study
Sustained-Release Dexamethasone Intravitreal Implant
in Diabetic Macular Oedema

Abstract: **The management of macular oedema has benefited in recent years from therapeutic advances with the development of anti-VEGF and intravitreal steroid implants. The therapeutic management of diabetic macular oedema (DMO), which until recently was only treated by using standard laser treatment, has been revolutionised with these new products. At present, only ranibizumab and fluocinolone have the marketing authorisation (MA) for this indication. However, a Marketing Authorisation Application (MAA) for this indication is in progress for Ozurdex which appears to be an effective treatment for decreased visual acuity secondary to DMO with an acceptable risk/benefit ratio. Patient monitoring must be tailored to the duration of the product's action, with a consultation at M1 to detect any hypertonia and M5 to check for a recurrence of DMO with decreased visual acuity.**

→ E.MATONTI, S. POMMIER, C. HAJJAR, E. PARRAT, P.Y. MERITE, O. PROST-MAGNIN, F. MEYER, S. GUIGOU, TEAM P1.5
Ophthalmology Department, Hôpital Nord, MARSEILLE

Diabetes, and in particular diabetic macular oedema (DMO), is one of the main causes of visual impairment and visual disability in industrialised countries. However, its treatment has benefited in recent years from the appearance of new therapies that have improved functional results and offered a better prognosis for this disease. Whereas the treatment of systemic factors (control of blood pressure, blood glucose and lipids) remains fundamental in the therapeutic strategy for DMO, laser and intravitreal injections (IVT) still have an essential complementary role in its global management.

Treatment of DMO

Laser maintains a central position in the treatment of focal oedema, but it has lost its dominant position in the management of diffuse oedema in favour of anti-VEGF IVT to which it may sometimes be associated. Anti-VEGF agents such as ranibizumab (Lucentis) can often bring a real functional benefit to the patient, although at the price of iterative injections. This raises the issue of cumulative side effects induced by the injected drugs: enophthalmia, retinal tears, etc. Furthermore, the risk of systemic side effects (cardiovascular) of anti-VEGF agents may be accentuated in the subjects already at risk. The use of drugs with sustained action such as long-acting steroids is attracting real interest. The triamcinolone acetonide IVTs have been used for several years to treat refractory DMO treated with laser. Several randomized trials have demonstrated the efficacy, at least in the short-term, of these triamcinolone IVTs in

Guigou S *et al. J Fr Ophthalmol* 2014;37:480–485.

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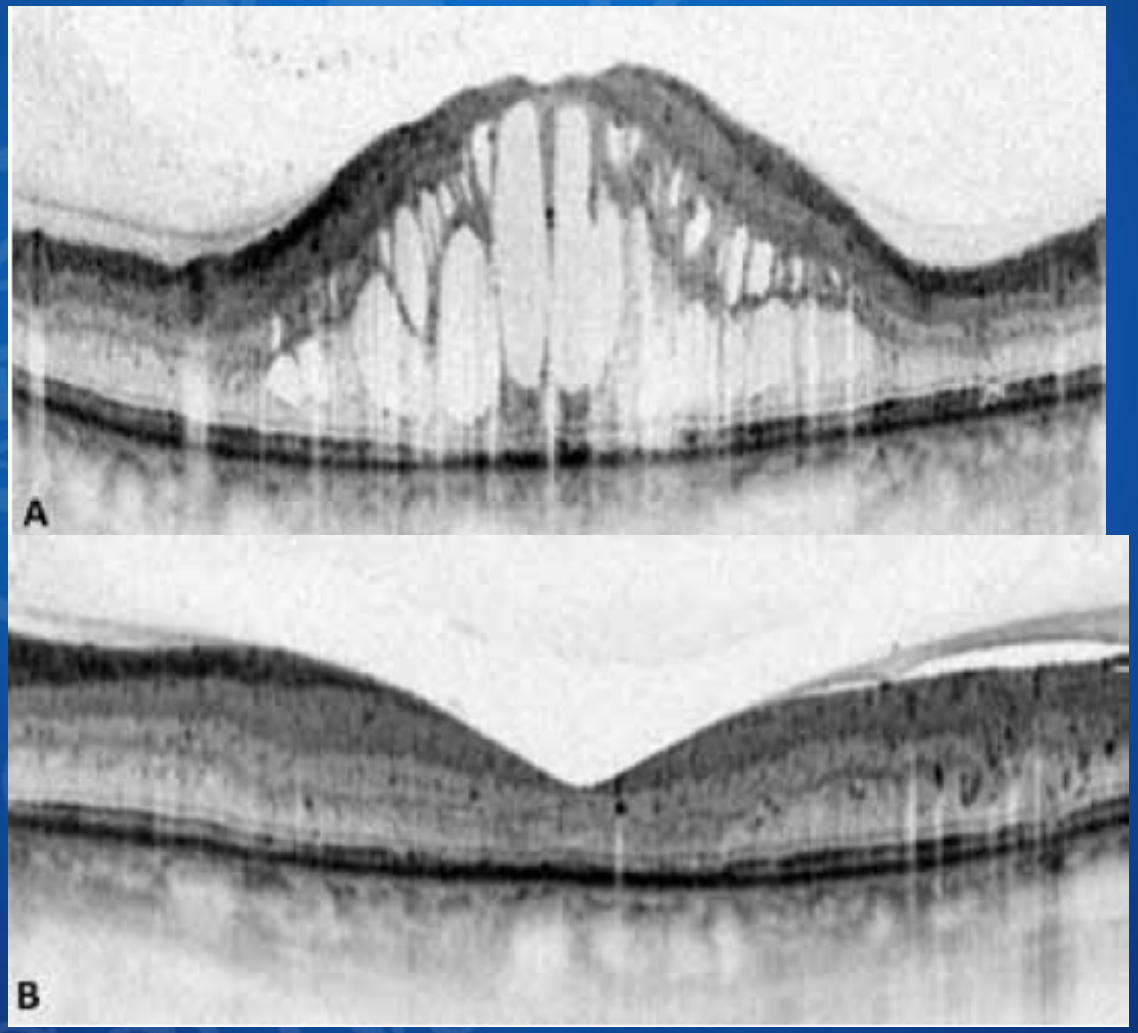
RISULTATI POST TRATTAMENTO



DME refrattario a grid laser e a 3aVEGF nell'anno precedente
VA 20/40
FT 740 μm

1 mese dopo DEX e stabile dopo mese 2
VA 20/70
FT 180 μm
NESSUN SEGNO DI EDEMA (75%_15 occhi)

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Valutazioni

Visus

- Stabilizzazione del visus:

  sopratutto nei pz pseudofachici

- Peggioramento:

  nei pz fachici a causa della cataratta!!

MEAD

MACULAR EDEMA:
ASSESSMENT OF IMPLANTABLE
DEXAMETHASONE IN DIABETES

Three-Year, Randomized, Sham-Controlled Trial of Dexamethasone Intravitreal Implant in Patients with Diabetic Macular Edema

*David S. Boyer, MD,[1] Young Hee Yoon, MD, PhD,[2] Rubens Belfort, Jr, MD, PhD,[3] Francesco Bandello, MD,[4] Raj K. Maturi, MD,[5] Albert J. Augustin, MD,[6] Xiao-Yan Li, MD,[7] Harry Cui, MS,[7] Yehia Hashad, MD,[7] Scott M. Whitcup, MD,[7] for the Ozurdex MEAD Study Group**

Purpose: To evaluate the safety and efficacy of dexamethasone intravitreal implant (Ozurdex, DEX implant) 0.7 and 0.35 mg in the treatment of patients with diabetic macular edema (DME).

Design: Two randomized, multicenter, masked, sham-controlled, phase III clinical trials with identical protocols were conducted. Data were pooled for analysis.

Participants: Patients (n = 1048) with DME, best-corrected visual acuity (BCVA) of 20/50 to 20/200 Snellen equivalent, and central retinal thickness (CRT) of ≥300 μm by optical coherence tomography.

Methods: Patients were randomized in a 1:1:1 ratio to study treatment with DEX implant 0.7 mg, DEX implant 0.35 mg, or sham procedure and followed for 3 years (or 39 months for patients treated at month 36) at ≤40 scheduled visits. Patients who met retreatment eligibility criteria could be retreated no more often than every 6 months.

Main Outcome Measures: The predefined primary efficacy endpoint for the United States Food and Drug Administration was achievement of ≥15-letter improvement in BCVA from baseline at study end. Safety measures included adverse events and intraocular pressure (IOP).

Results: Mean number of treatments received over 3 years was 4.1, 4.4, and 3.3 with DEX implant 0.7 mg, DEX implant 0.35 mg, and sham, respectively. The percentage of patients with ≥15-letter improvement in BCVA from baseline at study end was greater with DEX implant 0.7 mg (22.2%) and DEX implant 0.35 mg (18.4%) than sham (12.0%; $P \leq 0.018$). Mean average reduction in CRT from baseline was greater with DEX implant 0.7 mg (−111.6 μm) and DEX implant 0.35 mg (−107.9 μm) than sham (−41.9 μm; $P < 0.001$). Rates of cataract-related adverse events in phakic eyes were 67.9%, 64.1%, and 20.4% in the DEX implant 0.7 mg, DEX implant 0.35 mg, and sham groups, respectively. Increases in IOP were usually controlled with medication or no therapy; only 2 patients (0.6%) in the DEX implant 0.7 mg group and 1 (0.3%) in the DEX implant 0.35 mg group required trabeculectomy.

Conclusions: The DEX implant 0.7 mg and 0.35 mg met the primary efficacy endpoint for improvement in BCVA. The safety profile was acceptable and consistent with previous reports. *Ophthalmology 2014;121:1904-1914*

Supplemental material is available at www.aaojournal.org.

MEAD

Pazienti pseudofachici

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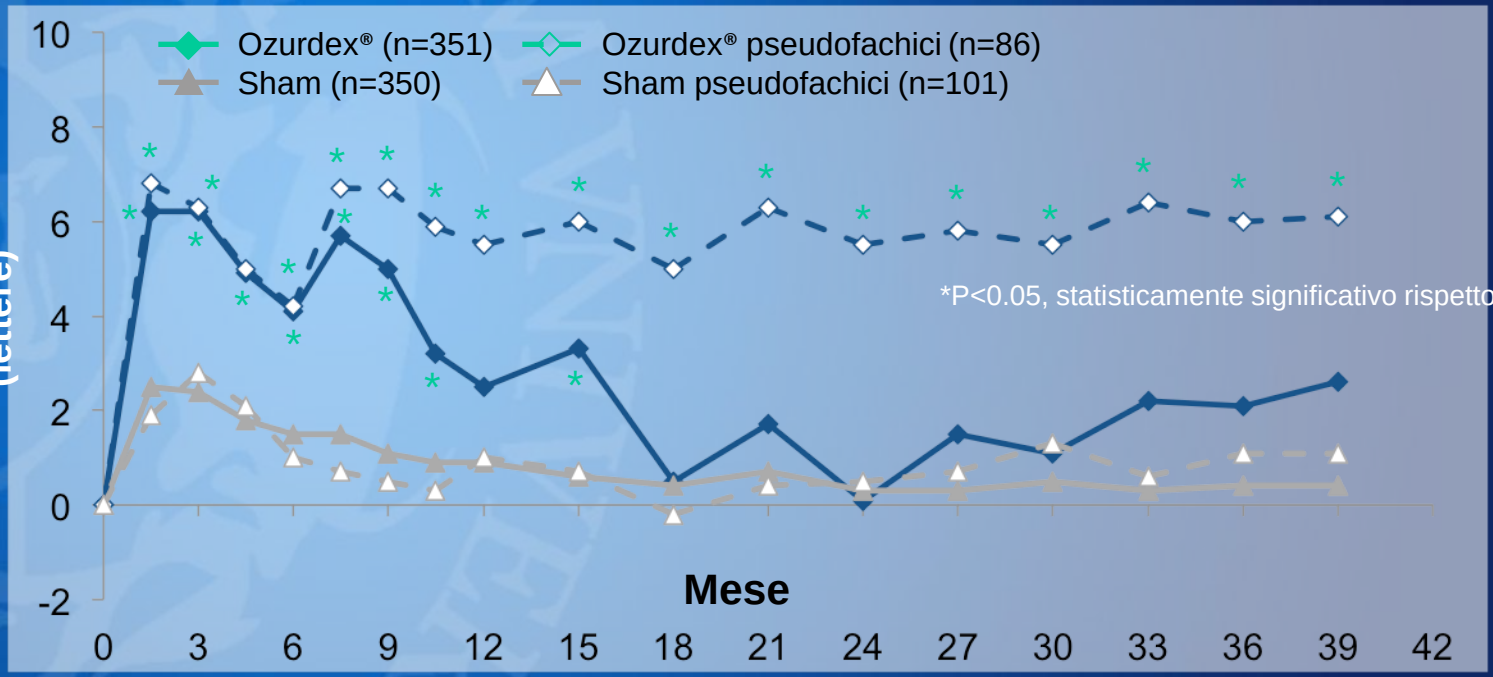
Variazione media della BCVA rispetto al basale



I pazienti che hanno ricevuto Ozurdex® hanno mostrato un maggior miglioramento della variazione media della BCVA durante lo studio rispetto alla sham
La cataratta confondeva le variazioni della BCVA al basale nei pazienti fachici dopo 1 anno, tuttavia con Ozurdex® si notavano ancora miglioramenti significativi per 3 anni

BCVA: acutezza visiva corretta al meglio; EMA: European Medicine's Agency

Boyer DS *et al. Ophthalmology* 2014 Jun 4.[Epub ahead of print]. DOI: 10.1016/jophtha.2014.04.024

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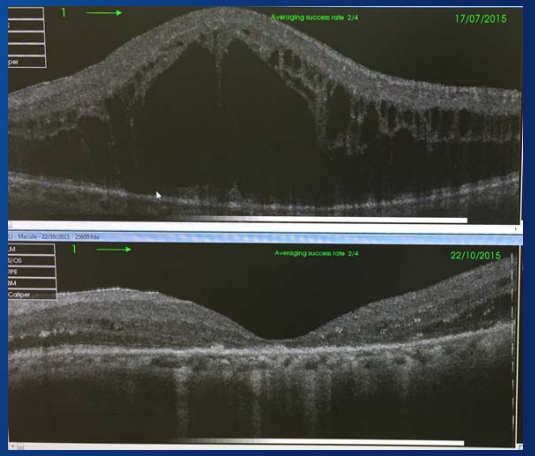
Valutazioni

Visus

Stabilita’ o peggioramento

- ✓ Perche' nessun pz naive?
- ✓ Perche' edemi cronici?
- ✓ Perche' atrofia maculare??



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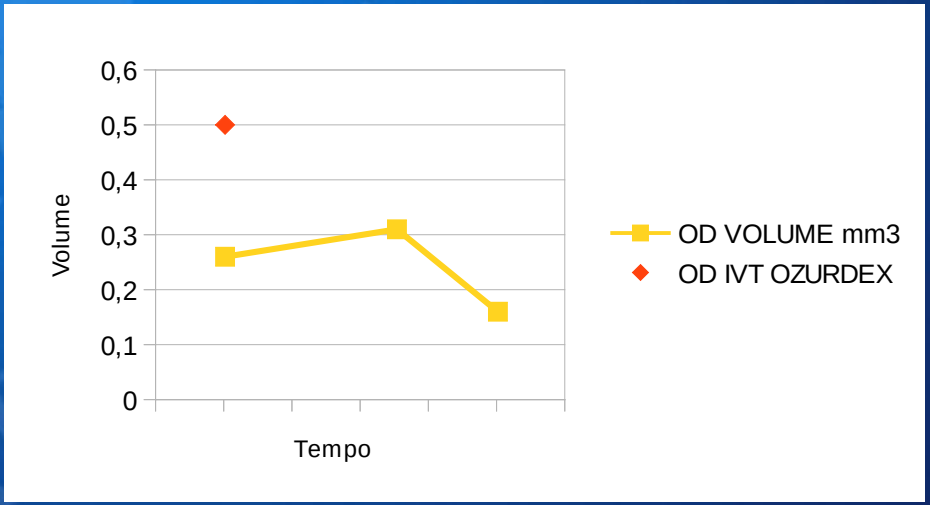
Valutazioni

Nei Pz vitrectomizzati

- Il numero di trattamenti e' minore rispetto ai pz non vitrectomizzati
- Bias del piccolo campione



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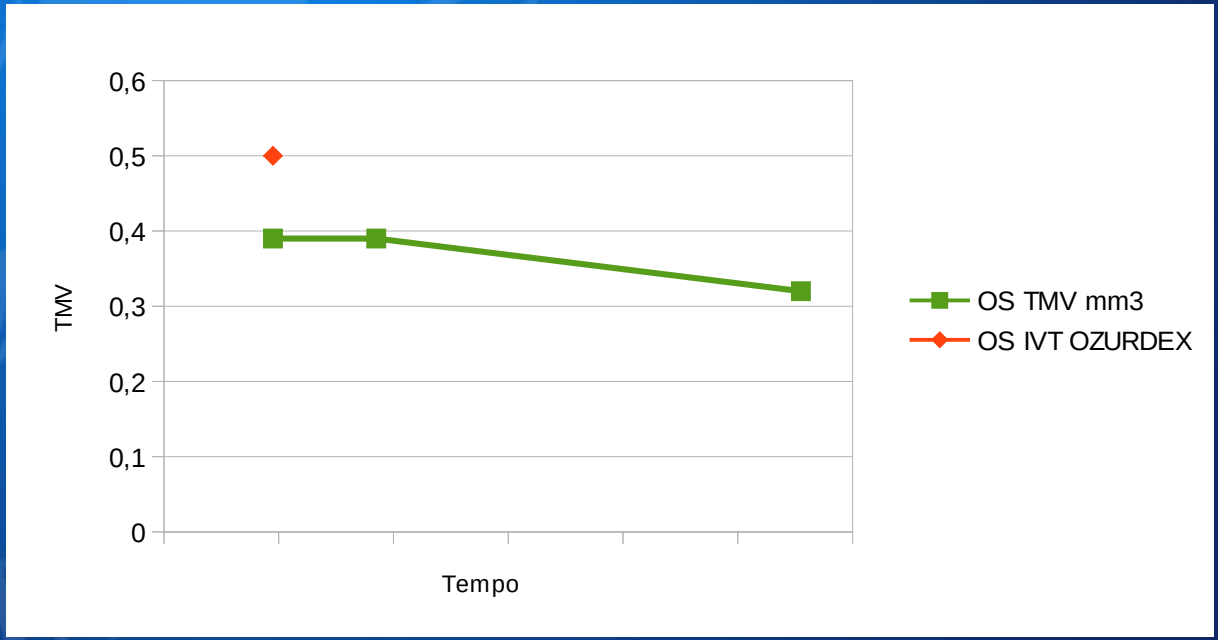
Valutazioni

Nei 4 pz vitrectomizzati il risultato anatomico e funzionale e' una stabilita' visiva con riduzione del TMV per un tempo maggiore gia' al primo trattamento.



Valutazioni

Quindi nei pz vitrectomizzati consideriamo sia :

- Ruolo della vitrectomia nell'edema diabetico
- Ruolo della flogosi nella patogenesi dell'edema

DEXAMETHASONE INTRAVITREAL IMPLANT FOR TREATMENT OF DIABETIC MACULAR EDEMA IN VITRECTOMIZED PATIENTS

DAVID S. BOYER, MD,* DAVID FABER, MD,† SUNIL GUPTA, MD,‡ SUNIL S. PATEL, MD, PhD,§ HOMAYOUN TABANDEH, MD,* XIAO-YAN LI, MD,¶ CHARLIE C. LIU, PhD,¶ JEAN LOU, MD, PhD,¶ SCOTT M. WHITCUP, MD,¶ FOR THE OZURDEX CHAMPLAIN STUDY GROUP

Purpose: To evaluate the safety and efficacy of Ozurdex (dexamethasone intravitreal implant) 0.7 mg in the treatment of diabetic macular edema in vitrectomized eyes.

Methods: This was a prospective, multicenter, open-label, 26-week study. Fifty-five patients with treatment-resistant diabetic macular edema and a history of previous pars plana vitrectomy in the study eye received a single intravitreal injection of 0.7-mg dexamethasone intravitreal implant. The primary efficacy outcome measure was the change in central retinal thickness from baseline to Week 26 measured by optical coherence tomography.

Results: The mean age of patients was 62 years. The mean duration of diabetic macular edema was 43 months. The mean (95% confidence interval) change from baseline central retinal thickness (403 μm) was −156 μm (−190, −122 μm) at Week 8 ($P < 0.001$) and −39 μm (−65, −13 μm) at Week 26 ($P = 0.004$). The mean (95% CI) increase in best-corrected visual acuity from baseline (54.5 letters) was 6.0 letters (3.9, 8.1 letters) at Week 8 ($P < 0.001$) and 3.0 letters (0.1, 6.0 letters) at Week 26 ($P = 0.046$). At Week 8, 30.4% of patients had gained ≥10 letters in best-corrected visual acuity. Conjunctival hemorrhage, conjunctival hyperemia, eye pain, and increased intraocular pressure were the most common adverse events.

Conclusion: Treatment with dexamethasone intravitreal implant led to statistically and clinically significant improvements in both vision and vascular leakage from diabetic macular edema in difficult-to-treat vitrectomized eyes and had an acceptable safety profile.

RETINA 31:915–923, 2011

Pars plana vitrectomy (PPV) is beneficial in many conditions including diabetic retinopathy (DR), diabetic macular edema (DME), retinal detachment, macular holes, macular pucker, and vitreous hemorrhage. In a recent study reported by the Diabetic Retinopathy Clinical Research Network, vitrectomy resulted in a decrease in retinal thickness in most eyes with DME and vitreomacular traction. After vitrectomy, 38% of the study eyes had increased visual acuity, while 22% had decreased visual acuity. Unless replaced by another viscous substance, such as silicone oil, removal of the vitreous leads to increased diffusion of substances to and from the retina.[1] In DR, both the delivery of oxygen to the retina and the removal of inflammatory mediators of DME, such as vascular endothelial growth factor (VEGF), from the retina are improved after vitrectomy.[1]

An unintended consequence of the procedure is that subsequent intravitreal pharmacologic treatment of posterior segment disease may be less effective in vitrectomized eyes. Drug diffusion and clearance from

From the *Retina-Vitreous Associates Medical Group, Los Angeles, California; †Rocky Mountain Retina Consultants, Salt Lake City, Utah; ‡Retina Specialists Pensacola, Pensacola, Florida; §Retina Research, Institute of Texas, Abilene, Texas; and ¶Allergan, Inc, Irvine, California.

Supported by Allergan, Inc (Irvine, CA).

X.-Y. Li, C. C. Liu, J. Lou, and S. M. Whitcup are employees of Allergan, Inc. D. S. Boyer, D. Faber, S. Gupta, S. S. Patel, and H. Tabandeh are consultants for Allergan, Inc.

The members of the Champlain Study Group are listed in the appendix.

Reprint requests: David S. Boyer, MD, Retina-Vitreous Associates Medical Group, 8641 Wilshire Boulevard, Suite 210, Beverly Hills, CA 90211; e-mail: vitdoc@aol.com

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Valutazioni

Aumento della pressione intraoculare

- L'impianto di Ozurdex in CV puo' causare un aumento della IOP comunque gestibile con terapia topica.
- Effetto collaterale presente nel 31,2% del nostro campione (vs 15,8% di letteratura).

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Conclusioni

Impianto di Ozurdex

come opzione terapeutica ?

- e' sicuramente valida in termini di stabilizzazione anatomica e funzionale
- selezione di pz

  ridotta compliance agli anti-VEGF

  controindicazioni agli anti-VEGF

  in pz naive e' maggiore l'efficacia ?

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Conclusioni

- Alto rischio di cataratta

  Pz pseudofachici

- Pz vitrectomizzati!!! [Boyer DS, Retina 2011]

- Costi: puo'essere un criterio di scelta?

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