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Early Efficacy and Tolerance of The Intravitreal Implant of Dexamethasone (Ozurdex) for Refractory and Treatment-Naïve Diabetic Macular Edema: A Prospective Study About 40 Patients

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Abstract **Case Report**

Introduction: Dexamethasone implant has proven to improve visual and anatomic outcomes in patients with persistent DME or resistant to anti-VEGF therapy, with a good safety profile. ***Objective:*** Investigate the efficacy and safety of the dexamethasone implant after 2 months and compare the outcome between naïve and refractory patients. ***Methods:*** Monocentric prospective study from August 2022 to February 2023. Inclusion criteria were BCVA⩽ 0.3 logMar and ERC ⩾ 300 um secondary to OMD. Our primary endpoints were BCVA gain and ERC after 2 months in the naïve and non-naïve groups. Secondary endpoints were treatment side effects. ***Results:*** 40 eyes, 21 naïve and 19 non-naïve, were included in the study. The sex ratio M/F was 1.1, and the mean age was 65.4 years. 8 patients were pseudophakic. Mean BCVA was 1.01 logMar at inclusion and 0.71 logMar at M2. VA gain was higher and more prolonged in the naïve group. Mean ERC was 532 µm at inclusion and 298 µm at M2. Elevation of IOP was noted in 2 patients and was controlled with only toping hypotensive agents. No serious complications were observed. ***Conclusion:*** The dexamethasone implant is effective in the treatment of DME, with a significant gain in VA and reduction in CME in both groups, with a good tolerance profile. Better visual and anatomic outcomes were observed in the treatment-naïve group.

Keywords: Diabetes, macular edema, Dexamethasone implant, treatment-naïve, refractory, tolerance.

INTRODUCTION

Diabetes is a chronic metabolic disease that leads to various microvascular and macrovascular complications. The number of individuals affected by diabetes miellitus is estimated to be around 700 millions worldwide. Diabetic macular edema (DME) is a serious complication which threatens the vision of patients with diabetic retinopathy. It is characterized by macular thickening due to the breakdown of the blood-retinal barrier, resulting in vascular leakage and extracellular fluid accumulation. This dysfunction results from the expression of inflammatory factors, notably vascular endothelial growth factor (VEGF), intercellular adhesion molecule-1, interleukin-6, monocyte chemoattractant protein-1, and leukostasis.

Its prevalence ranges from 4% to 14% among the diabetic population, depending on factors such as diabetes duration, severity of diabetic retinopathy, glycemic control, and associated hypertension. After 20 years of diabetes evolution, the prevalence of DME reaches 28%.

In addition to glycemic control, several therapeutic options are available for the management of DME, including laser photocoagulation, which was the mainstay treatment for DME over the last four decades. Advances in our understanding of DME pathophysiology have led to new treatments, such as anti-VEGF agents and corticosteroids. Anti-VEGF agents, either alone or in combination with laser photocoagulation, have become the first-line treatment for DME. Although the FDA has approved their use in

DME, a subset of patients shows resistance to treatment, and therapeutic compliance remains suboptimal due to the high frequency of injections required per year.

The Dexamethasone implant, through its anti-inflammatory, moderate anti-VEGF effects, and restoration of endothelial tight junctions, also improves the anatomical and functional outcomes in DME.

Dexamethasone, an anti-inflammatory agent, has the highest relative clinical efficacy among corticosteroids used in ophthalmologic practice.

The 0.7 mg intravitreal dexamethasone implant (Ozurdex) consists of micronized dexamethasone embedded in a biodegradable copolymer of lactic and glycolic acid, releasing the steroid gradually into the vitreous cavity over approximately six months.

In 2014, based on the MEAD study results, the FDA and most European countries approved Ozurdex for DME treatment. Multiple studies have shown that Ozurdex® can improve central macular thickness (CMT) and best-corrected visual acuity (BCVA) in patients with DME. Moreover, in eyes with DME, dexamethasone implants provide significant functional benefits as early as one month after injection.

The objective of our study is to evaluate the efficacy of the dexamethasone implant at its peak activity (2 months post-injection), compare the results between treatment-naïve and previously treated patients, and assess its safety profile.

MATERIALS AND METHODS

We conducted a prospective, monocentric study involving 40 eyes from 33 patients presenting with visual acuity decline secondary to diabetic macular edema (DME), who received a single intravitreal injection of a dexamethasone implant. The study took place in the Ophthalmology Department at Omar Drissi Hospital in Fez, between August 2022 and February 2023.

Patients were divided into two groups:
Group 1: treatment-naïve, with no history of intravitreal injections.

Group 2: non-naïve, with refractory macular edema following intravitreal anti-VEGF injections and who received

the dexamethasone implant at least one month after their last anti-VEGF injection.

Inclusion criteria were: age over 18 years, type 1 or 2 diabetes with HbA1c < 12%, best-corrected visual acuity (BCVA) ≤ 0.3 logMar, and central retinal thickness (CRT) ≥ 300 µm. Follow-up duration was at least 4 months.

Exclusion criteria included: proliferative diabetic retinopathy without prior adequate panretinal photocoagulation or complicated by iris neovascularization, vitreous hemorrhage, or tractional retinal detachment; ischemic maculopathy; macular edema from causes other than diabetes; uncontrolled glaucoma or cases requiring more than two hypotensive agents; thromboembolic events within the last 3 months; and pregnant or breastfeeding women. Patients with dense cataracts or those lost to follow-up were also excluded.

All patients underwent a comprehensive ophthalmologic examination including BCVA measurement in logMar, slit-lamp biomicroscopy with fundus examination, and intraocular pressure (IOP) measurement. Spectral-domain optical coherence tomography (SD-OCT) was performed using the TOPCON DRI OCT Triton with 6 radial 6-mm B-scans. DME was defined as CRT ≥ 300 µm on SD-OCT. OCT parameters analyzed included CRT, presence of DRIL (disorganization of the retinal inner layers), serous retinal detachment (SRD), IS/OS junction integrity, and intraretinal hyperreflective foci.

Refractory macular edema was defined as a BCVA gain of <5 letters and/or CRT reduction of <10% after a minimum of 3 anti-VEGF injections. Any responsive macular edema was excluded from the study.

All patients provided written informed consent prior to the injection.

Each patient received a single standard-protocol intravitreal dexamethasone implant injection and was examined every 4 weeks thereafter.

Our aim was to evaluate both functional and anatomical efficacy at 2 months after injection. Primary endpoints were BCVA gain and CRT reduction at 2 months (corresponding to the peak efficacy of dexamethasone) in both the treatment-naïve and previously treated groups, along with treatment-related adverse events.

Statistical analysis was performed using the Chi-square test to calculate proportions. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 40 eyes from 33 patients were included in the study: 21 eyes (52.5%) were treatment-naïve and 19 eyes (47.5%) were previously treated. The mean age of patients was 61.2 years, with a slight male predominance (M/F sex ratio = 1.2) in both groups. All patients had type 2 diabetes, with a mean HbA1c of 8.9%. Eight patients (24%) were pseudophakic, and one patient received a dexamethasone implant injection at the time of cataract surgery. Nineteen patients had panretinal photocoagulated proliferative diabetic retinopathy, three

had moderate non-proliferative diabetic retinopathy, and two had mild non-proliferative diabetic retinopathy.

Eight patients (20%) presented with a subfoveal serous retinal detachment (SRD) associated with DME; five patients (15%) had disorganization of the retinal inner layers (DRIL), and 18 patients (54.5%) showed irregularities of the outer retinal layers, particularly disruption of the IS/OS junction.

The mean IOP before injection was 16.3 mmHg. No patients were on IOP-lowering therapy at baseline.

The clinical and demographic characteristics at baseline in both groups are summarized in Figure 1.

In the previously treated group, 17 eyes had received bevacizumab injections and 2 eyes had received aflibercept. On average, the 19 previously treated eyes had undergone 4.3 anti-VEGF injections over a mean follow-up of 7 months before switching to dexamethasone. Eight patients (12 eyes) were switched after 3 injections due to insufficient anatomical or functional improvement. One patient was switched after 5 injections, two after 6 injections, and three after 8 injections.

BCVA deteriorated in the non-naïve group after the last anti-VEGF injection cycle, worsening from 0.7 logMar to 1.1 logMar. CRT increased from 435 ± 95 µm to 540 ± 146 µm post-injection. These eyes were classified as refractory and switched to dexamethasone treatment.

In the non-naïve group, BCVA improved from 1.1 ± 0.3 logMar at baseline to 1.0 ± 0.2 logMar at 1 month and to 0.9 ± 0.2 logMar at 2 months after Ozurdex injection. The average gain in visual acuity at 2 months (peak efficacy) was 2 lines, with 2 patients gaining more than 5 lines.

For these previously treated patients, mean CRT was 540 ± 146 µm at baseline and decreased to 313 ± 104 µm at month 2 — an average reduction of 226 µm. Only one patient showed <10% reduction in CRT after injection; this patient had previously received 5 anti-VEGF injections with no response, and a tractional component was suspected.

In the treatment-naïve group, BCVA improved from 0.92 ± 0.65 logMar at baseline to 0.62 ± 0.3 at 1 month and to 0.49 ± 0.4 at 2 months — a mean gain of 4.2 lines. Visual improvement was more marked and sustained in the treatment-naïve group compared to the previously treated group, with a statistically significant difference ($p = 0.02 < 0.05$).

Anatomically, mean CRT decreased from 525 ± 162 µm to 285 ± 170 µm at month 2, a mean reduction of 240 µm.

Figures 2 and 3 respectively illustrate BCVA (logMar) and CRT (µm) at 2 months in both groups.

Figure 4 summarizes the comparison of anatomical and functional outcomes at 2 months between groups.

Figure 5 demonstrates the anatomical response on B-scan OCT in a treatment-naïve patient, showing CRT reduction and regression of cystoid spaces at 2 months post-injection.

Anatomical improvement was observed in both groups, though it was more pronounced in the treatment-naïve group, without reaching statistical significance ($p > 0.05$).

There was no significant difference in BCVA gain or CRT reduction between phakic and pseudophakic patients. A total of 23% of patients achieved final BCVA better than 0.3 logMar (equivalent to 70 ETDRS letters).

CRT reduction was significantly greater in patients with SRD compared to those without ($p < 0.05$), though no difference in visual gain was noted between these subgroups. The improved anatomical outcome in the presence of SRD reinforces the role of inflammation in DME and identifies SRD as a predictor of good anatomical response.

Regarding intraretinal hyperreflective foci (HRF), there was no difference in anatomical or functional outcomes between patients with and without HRF.

Mean IOP increased by +4 ± 3 mmHg at peak efficacy, reaching an average of 18.9 mmHg at month 2.

Ocular hypertension occurred in only 2 patients (6%) and was controlled with single-agent hypotensive treatment. No patient developed uncontrolled IOP or required filtering surgery.

Mild to moderate cataract progression was observed in 30% of patients.

No serious complications were reported (e.g., endophthalmitis, retinal detachment, central retinal artery occlusion, cardiovascular events) during follow-up.

Figure 1: Table comparing baseline demographic and clinical features, for both the naïve and non naïve groups

	Naïve (n=21)	Non naïve (n=19)
Age	58.8	63.6
Gender (M/F)	12/9	10/6
Hb1ac (%)	8.6	9.2
PDR+PRP	11	8
BCVA (logMar)	0.9 +/- 0.15	1+/-0.3
CRT (um)	490	530
Main IOP (mmHg)	15.9	16.7

PDR : Proliferative diabetic retinopathy
PRP : Panretinal photocoagulation

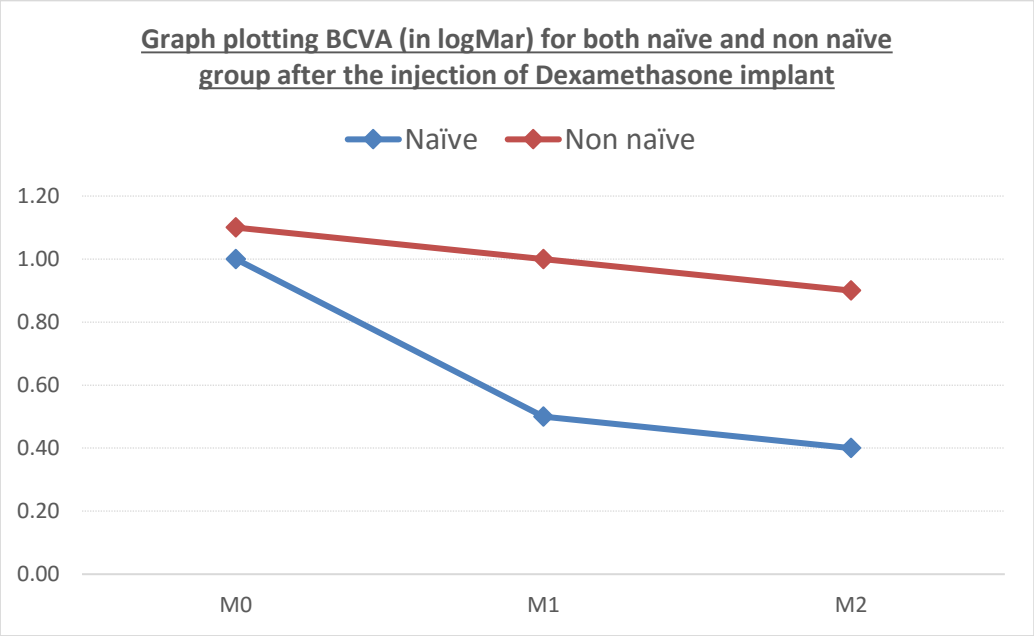

Figure 2

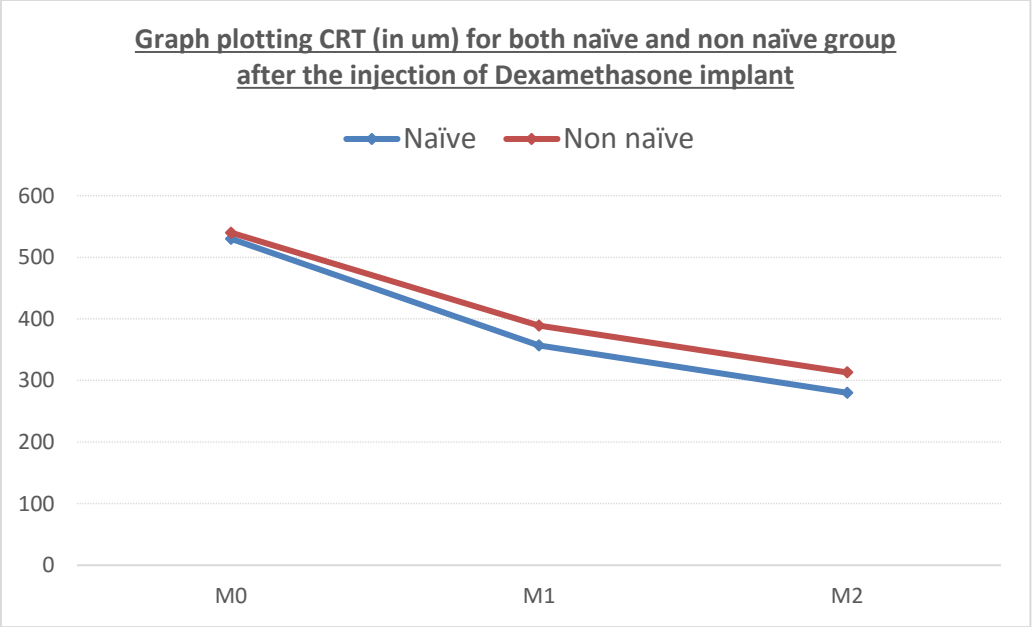

Figure 3

Figure 4: Table comparing functional and anatomical outcomes at 2 months, for both the naïve and non naïve groups

	Naïve	Non naïve	p
BCVA gain (logMar)	4.2	1.95	0.02 < 0.05
CRT reduction (um)	240	226	0.7 > 0.05

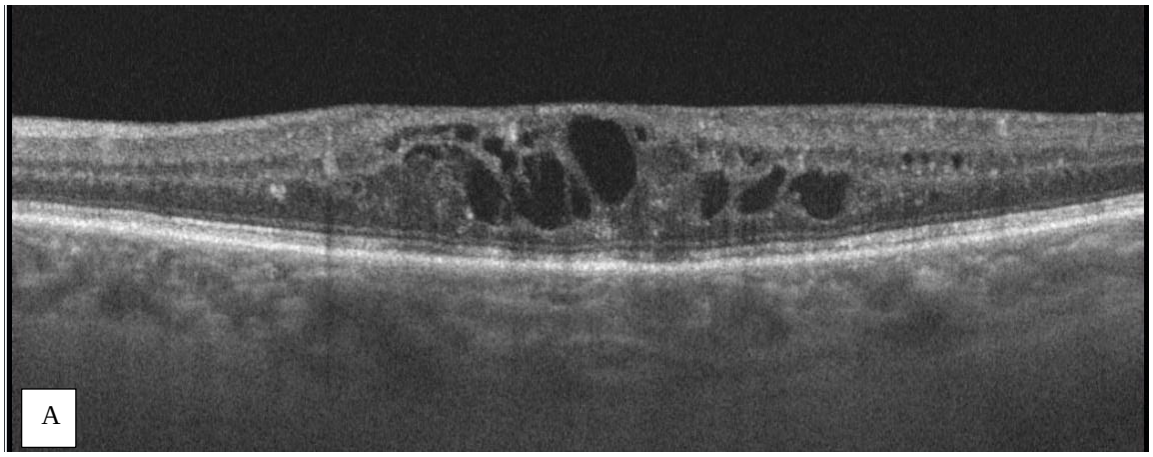

Figure 5 A: OCT B-scan of a 65-year-old treatment-naïve patient with diabetic retinopathy and macular edema with intraretinal cysts and ERC measured at 395um

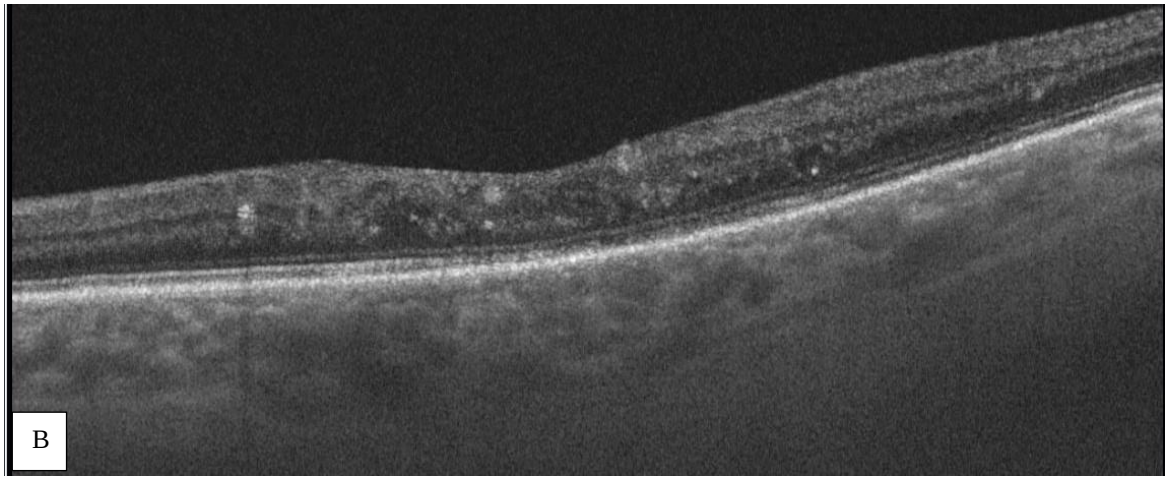

Figure 5 B: Anatomical response after Dexamethasone implant, showing CRT reduction and regression of cystoid spaces at 2 months post-injection.

DISCUSSION

The efficacy of Ozurdex® has been well established in clinical studies, with an average of 2 to 3 intravitreal injections (IVT) required during the first year. In the RELDEX study, this efficacy was sustained over time, with a gain of +9.5 letters maintained at 3 years and a non-significant reduction in the number of IVT per year.

In our study of 40 eyes from 33 patients with DME, including 21 treatment-naïve and 19 previously treated eyes (mostly with bevacizumab, 95%), we observed significant improvements in both anatomical and functional outcomes following dexamethasone implant injection in both groups.

Specifically, the average BCVA gain was 2.7 lines at 2 months post-injection, accompanied by a mean CRT reduction of 233 µm. Functional improvement was significantly more pronounced in treatment-naïve patients ($p < 0.05$). Functional recovery is likely influenced by damage to the inner and outer retina, which is often associated with chronic edema. As for anatomical improvement, CRT decreased in both groups, though the difference was not statistically significant ($p > 0.05$). This finding aligns with most published studies showing greater visual gain and more marked CRT reduction in treatment-naïve patients.

The dexamethasone implant was well tolerated in our study, with only two cases of ocular hypertension during follow-up, both controlled with single-agent topical therapy. No serious adverse events were reported.

A review of previous studies on the efficacy and safety of the dexamethasone implant found similar results to ours. Studies by Wang *et al.,* Majstruk *et al.,* Castro Navarro *et al.,* and the RELDEX study all compared Ozurdex efficacy in treatment-naïve and previously treated patients. They showed a significantly greater functional improvement in the treatment-naïve group, with a gain of more than 3 lines of BCVA and final VA >20/40 in a higher proportion of patients ($p < 0.05$). Anatomical improvement was observed in both groups, with no significant difference during follow-up. Regarding safety, no severe complications were reported. In Wang *et al.*'s series, 25% of patients had IOP >20 mmHg, which was successfully managed with medical treatment alone. In Castro Navarro *et al.*'s study, DME subtype (diffuse, cystoid, or SRD) did not influence functional improvement, but anatomical improvement was significantly greater in the subgroup with SRD—this result was also observed in our study and may be explained by a higher baseline CRT in these patients.

In Sarda *et al.*'s study, the patient characteristics were similar to those in our cohort, with a mean age of 67 years compared to 61.2 years in our study. The primary endpoint in their study—BCVA gain—was also evaluated at 2 months (peak efficacy), as in our series. The average number of anti-VEGF IVTs in the previously treated group was 9.06 before switching, which is higher than in our study (4.6 injections on average). Good anatomical and functional responses were observed in the previously treated group, with a BCVA gain of 7.7 letters and a CRT reduction of 277.7 µm. A total of 57.89% of patients had CRT <300 µm at month 2, which is similar to our result (CRT <300 µm in 65% at month 2). Among the three treatment-naïve patients in their study, BCVA gain exceeded 15 ETDRS letters, but the sample size was too small to be significant. Regarding adverse effects, cataract surgery was performed in one case due to lens opacification, and two patients had IOP >25 mmHg without requiring filtering surgery.

The IRGREL-DEX study is an international, retrospective, multicenter study comparing DME patients who were treatment-naïve versus those refractory to at least three monthly anti-VEGF injections. Its findings align with those of previous studies in terms of functional improvement, with post-injection CRT remaining higher in the previously treated group throughout follow-up.

Cataract, ocular hypertension, and endophthalmitis were the main concerns associated with intravitreal bi corticosteroid injections. Only one case of endophthalmitis (0.03%) was reported among 2,897 dexamethasone implant injections across 31 studies. IOP elevation requiring hypotensive treatment occurred in 14% to 41.5% of DME patients in multiple studies. In the MEAD trial, only 0.6% of patients developed refractory ocular hypertension requiring filtering surgery.

CONCLUSION

This study suggests the intravitreal dexamethasone implant (Ozurdex) is effective in the treatment of DME, with significant VA gain and CME reduction in both the naive group, and the one refractory to anti-VEGF, with a more pronounced and prolonged improvement in the naive group. Our study has also proven the Ozurdex implant had a great tolerance profile with a low complication rate observed in our patients. This implant seems to be an effective long term alternative, requiring very few 'IVTs' over time and having a good safety profile. Its use in our context is unfortunately still constrained by its highcost.

REFERENCES

1. UK Prospective Diabetes Study (UKPDS). VIII. Study design, progress and performance. Diabetologia. 1991;34:877–890.
2. Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: pathogenesis and treatment. Surv Ophthalmol. 2009;54(1):1–32.
3. Funatsu H, Noma H, Mimura T, Eguchi S, Hori S. Association of vitreous inflammatory factors with diabetic macular edema. Ophthalmology. 2009; 116(1):73–9.
4. A Girach 1, H Lund-Andersen Diabetic macular oedema: a clinical overview.
5. R Klein, B E Klein, S E Moss, M D Davis, D L DeMets The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years.
6. Ford JA, Lois N, Royle P, Clar C, Shyangdan D, Waugh N. Current treatments in diabetic macular oedema: systematic review and meta-analysis. BMJ Open. 2013;3(3).
7. He Y, Ren XJ, Hu BJ, Lam WC, Li XR. A meta-analysis of the effect of a dexamethasone intravitreal implant versus intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema. BMC Ophthalmol. 2018;18(1):121.
8. Zhang L, Wang W, Gao Y, Lan J, Xie L. The Efficacy and Safety of Current Treatments in Diabetic Macular Edema: A Systematic Review and Network Meta-Analysis. PLoS One. 2016;11(7):e0159553.
9. Das A, McGuire PG, Rangasamy S. Diabetic Macular Edema: Pathophysiology and Novel Therapeutic Targets. Ophthalmology. 2015;122(7):1375–94.
10. Pacella E, La Torre G, Impallara D, Malarska K, Turchetti P, Brillante C, et al. Efficacy and safety of the intravitreal treatment of diabetic macular edema with pegaptanib: a 12-month follow-up. Clin Ter. 2013;164(2):e121–6.

11. Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, Feiner L, et al. RISE and RIDE research group. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. Ophthalmology. 2012; 119(4):789–801.
12. Brown DM, Nguyen QD, Marcus DM, Boyer DS, Patel S, Feiner L, et al. RIDE and RISE Research Group. Long-term outcomes of ranibizumab therapy for diabetic macular edema: the 36-month results from two phase III trials: RISE and RIDE. Ophthalmology. 2013;120(10):2013–22.
13. Haghjou N, Soheilian M, Abdekhodaie MJ. Sustained release intraocular drug delivery devices for treatment of uveitis. J Ophthalmic Vis Res. 2011; 6(4):317–29.
14. Chang-Lin JE, Attar M, Acheampong AA, Robinson MR, Whitcup SM, Kuppermann BD, et al. Pharmacokinetics and pharmacodynamics of a sustained-release dexamethasone intravitreal implant. Invest Ophthalmol Vis Sci. 2011;52(1):80–6.
15. Boyer DS, Yoon YH, Belfort R Jr, Bandello F, Maturi RK, Augustin AJ, et al. Ozurdex MEAD study group. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. Ophthalmology. 2014;121(10):1904–14.
16. Iglicki M, Busch C, Zur D, Okada M, Mariussi M, Chhablani JK, et al. DEXAMETHASONE IMPLANT FOR DIABETIC MACULAR EDEMA IN NAIVE COMPARED WITH REFRACTORY EYES: the international retina group real-life 24-month multicenter study. The IRGREL-DEX study. Retina. 2018.
17. Mastropasqua R, Toto L, Borrelli E, Di Antonio L, De Nicola C, Mastrocola A, Di Nicola M, Carpineto P. Morphology and Function over a One-Year Follow Up Period after Intravitreal Dexamethasone Implant (Ozurdex) in Patients with Diabetic Macular Edema. PLoS One. 2015;10(12):e0145663.
18. Malclès A, Dot C, Voirin N, Agard É, Vié AL, Bellocq D, et al. Real-life study in diabetic macular edema treated with dexamethasone implant: The Reldex Study. Retina 2017;37:753–60.
19. Jia-Kang Wang a,b,c,d,e,*,Tzu-Lun Huanga,b, Yung-Ray Hsua,e, Pei-Yao Changa, Effect of dexamethasone intravitreal implant for refractory and treatment-naive diabetic macular edema in Taiwanese patients.
20. Verónica Castro-Navarro1,2*, Enrique Cervera-Taulet1 , Catalina Navarro-Palop1 , Clara Monferrer-Adsuara1 , Laura Hernández-Bel1 and Javier Montero-Hernández Intravitreal dexamethasone implant Ozurdex® in naïve and refractory patients with different subtypes of diabetic macular edema.
21. L. Majstruk, L. Qu-Knafo, V. Sarda, F. Fajnkuchen, S. Nghiem-Buffet, T. Grenet, G. Chaine, A. Giocanti-Auregan Dexamethasone intravitreal implant (Ozurdex) in patients with diabetic macular edema: Real life safety and efficacy.
22. V. Sarda a, F. Fajnkuchen a b, S. Nghiem-Buffet a b, T. Grenet a b, G. Chaine a, A. Giocanti-Auregan Early efficacy of dexamethasone implant (OZURDEX®) in diabetic macular edema: Real life study.
23. DEXAMETHASONE IMPLANT FOR DIABETIC MACULAR EDEMA IN NAIVE COMPARED WITH REFRACTORY EYES: The International Retina Group Real-Life 24-Month Multicenter Study. The IRGREL-DEX Study Matias Iglicki 1, Catharina Busch 2, Dinah Zur 3 4, Mali Okada 5, Miriana Mariussi 6, Jay Kumar Chhablani 7, Zafer Cebeci 8, Samantha Fraser-Bell 9, Voraporn Chaikitmongkol 10, Aude Couturier 11, Ermete Giancipoli 12, Marco Lupidi 13, Patricio J Rodríguez-Valdés 14, Matus Rehak 2, Adrian Tien-Chin Fung 15 16 17, Michaella Goldstein 3 4, Anat Loewenstein.
24. Kodjikian L, Bellocq D, Mathis T. Pharmacological management of diabetic macular edema in real-life observational studies. Biomed Res Int 2018;2018:8289253.