Safety of intravitreal dexamethasone implant (ozurdex): the safodex study. incidence and risk factors of ocular hypertension

MALCLES, Ariane, et al.

Abstract
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Reference

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SAFETY OF INTRAVITREAL DEXAMETHASONE IMPLANT (OZURDEX)

The SAFODEX study. Incidence and Risk Factors of Ocular Hypertension

ARIAINE MALCLÈS, MD,* CORINNE DOT, MD, PhD,†‡ NICOLAS VOIRIN, PhD,* ANNE-LAURE VIÉ, MD,* ÉMILIE AGARD, MD,†‡ DAVID BELLOCQ, MD,* PHILIPPE DENIS, MD, PhD,* LAURENT KODJIKIAN, MD, PhD*

Purpose: To analyze the incidence, risk factors, and time course of intraocular pressure elevation after intravitreal dexamethasone implant (Ozurdex).

Methods: The medical charts of 421 consecutive eyes (361 patients) receiving one or more Ozurdex implant between October 2010 and February 2015 were reviewed retrospectively. Ocular hypertension was defined as intraocular pressure of at least 25 mmHg or an increase of at least 10 mmHg from baseline. The main indications for treatment were retinal vein occlusion (34%), diabetic macular edema (30%), postsurgical macular edema (17%), uveitis (14%), and other etiologies (5%).

Results: Among 1,000 intravitreal injections, ocular hypertension was recorded for 28.5% of injected eyes over a mean follow-up period of 16.8 months (3–55). Intraocular pressure-lowering medication was required for 31% of eyes. Only three eyes with preexisting glaucoma required filtering surgery to manage postinjection intraocular pressure elevation. Early retreatment between the third and fourth month does not increase the risk of intraocular pressure elevation. Younger age, male sex, Type 1 diabetes, preexisting glaucoma treated with dual or triple therapy, and a history of retinal vein occlusion or uveitis were significant risk factors for ocular hypertension after dexamethasone implant injection ($P < 0.05$ for all the above).

Conclusion: Episodes of ocular hypertension after Ozurdex implant were generally transient and successfully managed with topical treatment. An analysis of the risk factors may help to determine the risk–benefit ratio for individual patients treated with dexamethasone implants.

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S teroid-response ocular hypertension (OHT) was described by François1 and Mac Lean2 in the 1950s. All forms of corticosteroids (systemic, topical, periocular, intravitreal) can cause OHT.

The mechanisms involved in IOP elevation are complex, any modification or blockage of the ultrastructure of the trabecular meshwork can hinder the outflow of aqueous humor, thus causing a rise in IOP. Corticosteroids inhibit proteases and the phagocytosis of the trabecular cells, which reduce damage to the extracellular matrix of the trabecular meshwork. These modifications to the trabecular microstructure, which increase resistance to the drainage of the aqueous humor, also cause a reduction in filtration, which in turn increases IOP.3

Intravitreal injections of Ozurdex (Allergan Inc, Irvine, CA) are an increasingly popular solution for treating macular edema (ME) secondary to RVO,4 diabetic macular edema (DME),5 postsurgical ME,6 and uveitis.7 Along with cataracts, OHT is the most common

From the *Department of Ophthalmology, Croix-Rousse University Hospital, Hospices Civils de Lyon, UMR-CNRS 5510 Mateïs, University of Medicine Lyon 1, Lyon, France; †Department of Ophthalmology, Desgenettes Military Hospital, Lyon, France; and ‡French Military Health Service Academy, Val de Grâce, Paris, France.

N. Voirin is an independent biostatistician paid by Acropol, a non-profit organization (L. Kodjikian). C. Dot is a consultant for Bayer, Alcon, Allergan, and Novartis. P. Denis is a consultant for Allergan. L. Kodjikian is a consultant for Alcon, Allergan, Alimera, Bayer, Novartis and Thèa. The remaining authors have no any financial/conflicting interests to disclose.

Reprint requests: Laurent Kodjikian, MD, PhD, Department of Ophthalmology, Croix-Rousse University Hospital, Hospices Civils de Lyon, 103, Grande Rue de la Croix-Rousse, 69317 Lyon Cedex 04, France; e-mail: kodjikian.laurent@wanadoo.fr

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adverse effect of dexamethasone implants (DEX-I), although this hypertension seems to be better tolerated compared with other intravitreal corticosteroids currently available (triamcinolone acetonide, fluocinolone acetonide). Episodes of OHT are usually transient and successfully controlled with topical treatment. Although numerous studies have investigated the efficacy and tolerance of the Ozurdex implant, no studies to date have studied the predictive risk factors for IOP elevation after intravitreal injection of DEX-I.

This study aimed to analyze the pressure tolerance of Ozurdex used in “real-life” conditions. The objective was to report the incidence of OHT, to analyze the pressure tolerance profile according to the different pathologies treated in the study cohort, and to identify possible risk factors for the onset of OHT after DEX-I injection.

Materials and Methods

Study Design

A descriptive, observational, retrospective, consecutive, uncontrolled multicenter series was conducted in the ophthalmology unit of the Croix-Rousse teaching hospital and the Desgenettes military hospital in Lyon. As the data were collected retrospectively and patient management was not modified, this study did not require research ethics committee approval, in compliance with French law (n°2004-806, August 9, 2004). It was conducted in accordance with the law on data protection (n°2004-801, August 6, 2004).

All consecutive patients presenting with at least one intravitreal injection of DEX-I 0.7 mg (Ozurdex) from October 2010 to February 2015 were included in this study.

The data collected on inclusion and at each follow-up consultation were history of OHT or primary open-angle glaucoma, IOP, and whether the patient was receiving IOP-lowering treatment.

Ocular hypertension was defined as IOP ≥25 mmHg or an increase of ≥10 mmHg over the follow-up period compared with baseline IOP.

Using the categories established by Becker, the patients were identified as “non or low responders” (increase of <6 mmHg), “intermediate responders” (increase of +6 to +15 mmHg), or “high responders” (increase of >15 mmHg) based on the largest increase in pressure measured in the three months after DEX-I.

Statistical Analysis

The description of the categorical variables was based on absolute frequencies (size) and relative frequencies (percentage). All quantitative variables are described using the mean and the SD.

The comparison of the categorical variables between the groups of different indications was performed using Fisher’s exact test, and when the pairwise comparisons were subsequently performed the P-value was adjusted using Benjamini & Hochberg’s method, because of the large number of statistical tests.

The factors associated with a risk of OHT were determined using logistic regression. A univariate analysis was performed. The variables with a P-value of <0.25 in the univariate analysis were included in the multivariate analysis. The results are presented with the adjusted or unadjusted odds ratio (OR) and the confidence interval. An OR >1 indicates a higher risk of hypertension. A P-value of <0.05 was considered to be statistically significant.

Results

A total of 421 eyes were analyzed in 361 patients. A total of 1,000 injections of Ozurdex were administered over the course of the study. The indications for the treatment were: ME secondary to RVO (n = 142), DME (n = 128), postsurgical ME (n = 73), uveitis (n = 58), and other etiologies (n = 20) (Table 1).

Forty-nine percent of patients were men. The mean age was 67 years (range 10–92) and 52% of eyes were pseudophakic at baseline.

Fourteen percent of patients (n = 58) had preexisting OHT or primary open-angle glaucoma at inclusion.

The mean follow-up period was 16.8 months (range 3–55 months). Patients received a mean of 2.4 DEX-I (range 1–11). Fifty-eight percent of eyes were retreated and a third of the cohort received at least three Ozurdex implants.

Only 11 eyes (5 DME and 6 RVO) required rescue treatment (intravitreal injections of anti–vascular endothelial growth factor) because of insufficient efficacy, and 3 other eyes (2 DME and 1 RVO) were treated with anti–vascular endothelial growth factor therapy for proliferative retinopathy during the study period. No patients received intravitreal injection of triamcinolone.

Furthermore, 16 patients with uveitis (25 eyes) were treated with systemic corticosteroids at some point during the follow-up period, including 4 patients (7 eyes) who received doses of less than or equal to 5 mg/day.

Incidence of Ocular Hypertension During Follow-up

The percentage of patients who developed OHT over the follow-up period (IOP ≥25 mmHg or an increase of ≥10 mmHg compared with baseline IOP) was 28.5%
Ocular hypertension of ≥25 mmHg occurred in 20% of cases (n = 85). This percentage dropped to 6% for hypertension of ≥35 mmHg (n = 24). Over the course of the follow-up period, 27% of eyes experienced an increase in pressure of ≥10 mmHg compared with their baseline IOP (n = 114).

The proportion of patients who developed OHT while treated with Ozurdex (IOP ≥25 or increase of ≥10 compared with baseline IOP) was higher in the RVO (36%) and uveitis (38%) groups than in the postsurgical ME (27%) and DME (17%) groups (Figure 1). This difference was statistically significant for the DME group compared with the RVO group (P = 0.006) and the DME group compared with the uveitis group (P = 0.009).

**Pressure Response According to Pathology**

The mean increase in IOP after the first DEX-I was +4.2 mmHg (uveitis +5.5 mmHg, RVO +4.7 mmHg, postsurgical ME +4.5 mmHg, and DME +2.5 mmHg). This increase is significantly lower in the DME group compared with the uveitis group (P = 0.045), and in the DME group compared with the RVO group (P = 0.01).

The analysis of the pressure response in the three months after the DEX-I injection found a higher proportion of intermediate (+6 to +15 mmHg) and high responders (+15 mmHg) in the RVO and uveitis groups (52% and 56%, respectively) compared with patients with DME and postsurgical ME (36% and 43%, respectively) (Figure 2). This difference was statistically significant for the DME group compared with the RVO group (P = 0.018), and the DME group compared with the uveitis group (P = 0.018).

**Subgroup of Patients With Ocular Hypertension or Glaucoma on Inclusion**

The analysis of the subgroup of patients with glaucoma/OHT at inclusion (n = 58) (baseline IOP = 13.5 mmHg ± 3.7) found poor pressure tolerance for patients with glaucoma treated with dual or triple therapy at baseline, with 50% and 100% of high responders to intravitreal DEX-I, respectively (Figure 3), and a 73% rate of OHT of ≥25 mmHg over the course of the follow-up period.

Thirty-seven percent of the patients with glaucoma treated with a monotherapy experienced IOP elevation of ≥25 mmHg during follow-up.

Patients treated for OHT or with a history of filtration surgery on inclusion seemed to have better tolerance, as the rate of hypertension of ≥25 mmHg was 8% and 17%, respectively in these 2 groups (P = 0.018).

**Postintravitreal Injection Peak Intraocular Pressure**

Ocular hypertension (IOP ≥25 mmHg) was most frequently diagnosed two months’ postintravitreal injection of DEX-I (51%), however, in some patients we also observed much earlier increases in pressure
(IOP $\geq 25$ mmHg) as of day 8 (12%), or at one month (23%), or later increases up to the third month (14%). The time to the onset of OHT is similar regardless of the number of intravitreal injections (IVT) (i.e., does not depend on the number of IVT, $P$-value = 0.5135).

**Management of Ocular Hypertension**

For 31% of eyes it was necessary either to introduce or add treatment with IOP-lowering eye drops during the follow-up period ($n = 129$) (Figure 1).

In most cases (97%), IOP elevation was successfully managed with topical treatment alone. Further treatment with oral acetazolamide (Diamox) was required for 14 patients (3%) including 5 with glaucoma (7 with RVO, 5 with uveitis, and 2 with postsurgical ME). No patients underwent selective laser trabeculoplasty.

Three patients required filtration surgery by trabeculectomy for persistent, uncontrolled OHT (0.7%); all these patients had glaucoma treated with dual ($n = 2$) or triple ($n = 1$) therapy at baseline.

In 6% of cases ($n = 24$), the onset of OHT led to the stopping of Ozurdex injections because of poor pressure tolerance (9% RVO, 7% uveitis, 4% postsurgical ME, and 2% DME). The IOP criteria for stopping DEX-I injections were not predefined and were left to the discretion of the treating clinicians.

**After How Many DEX-I Does IOP Increase?**

In responding patients (intermediate or high responders with an increase of $\geq 6$ mmHg), the first increase in IOP was diagnosed as of the first injection in 73% of cases (which increases to 87% if the first and second injection are taken into consideration). The proportion of “late responders” in which the first increase in pressure (increase of $\geq 6$ mmHg) was diagnosed at the third injection or later, was 13% (Table 2). Sixty-six percent of cases of IOP of $\geq 25$ mmHg were observed at the first injection (81% if the first and second injections are taken into consideration), and 19% of cases of OHT (first increase in pressure with IOP of $\geq 25$ mmHg) were diagnosed at a later stage.

Regarding the “late” cases of initial pressure increases with an IOP of $\geq 25$ mmHg ($n = 14$), 10 of these cases were not predictable, with IOP increasing dramatically despite there being no increase in pressure on administration of the previous DEX-I. In the other four cases, IOP seemed to increase more gradually with small increases in pressure at each injection.

**Repeat Injections and the Risk of Ocular Hypertension. Is There a Cumulative Effect?**

The number of patients with OHT decreased over the course of the follow-up period as patients received more DEX-I. The percentage of patients with IOP of $\geq 25$ mmHg was 5.6% at 2 months, 5% at 12 months, 2% at 24 months, and 4.3% at 36 months.

Figure 4 shows the mean IOP for “multi-injected eyes” (eyes, which have been administered 4 or more Ozurdex implants) over the duration of follow-up ($n = 86$).
The analysis of the 77 cases of early retreatment (with a further injection administered between 3–4 months after the previous one) found no additional risk of pressure elevation (increase ≥6 mmHg) compared with a time to retreatment of >4 months (18% pressure elevation with an increase of +6 mmHg) compared with 17% (P = 0.87).

**Risk Factors of Ocular Hypertension**

The univariate analysis identified the following risk factors for OHT after DEX-I: age ≥60 years (P < 0.001), male sex (P = 0.001), the etiologies RVO (P = 0.001) and uveitis (P = 0.003), preexisting glaucoma treated with dual or triple therapy (P = 0.010), and myopia with an axial length of >25 mm (P = 0.033). Lens (phakic/pseudophakic) and vitreous (vitrectomized or not) status do not affect the risk of OHT. Type 2 diabetes seems to have a protective effect (P < 0.001) with less OHT in these patients (Table 3).

Six independent risk factors were identified in the multivariate analysis. These were age ≥60 years (OR = 2.94, P < 0.001), male sex (OR = 2.24, P = 0.001), RVO (OR = 3.01, P = 0.011), and uveitis (OR = 3.26, P = 0.017), and glaucoma treated with dual or triple therapy (OR = 3.70, P = 0.017). Type 1 diabetes also seems to be a risk factor for OHT (OR = 8.07, P = 0.010).

**Reproducibility of the Pressure Response in Cases of Bilateral Injections**

Sixty patients were given bilateral injections over the follow-up period. Of these patients, 12 (20%) were found to have unilateral OHT (IOP ≥25 mmHg or increase ≥10 mmHg compared with baseline IOP). In 58% of cases, both eyes came under the same response category. The difference in pressure elevation between the 2 eyes after the first DEX-I was ≤3 mmHg in 62% of cases (n = 37), ≤5 mmHg in 83% of cases (n = 50), between 6 mmHg and 15 mmHg in 13% of cases (n = 8), and >15 mmHg in 3% of cases (n = 2).

A large difference in pressure elevation between the two eyes was found for only two patients during the follow-up period: one eye was a low responder and the fellow eye was a high responder. The first patient was treated for bilateral sarcoid uveitis. The second was a glaucoma patient treated for bilateral RVO. In this second patient, the low responder eye had previously undergone filtration surgery, whereas the fellow, high responder eye was being treated with triple pressure-lowering therapy at baseline.

**Discussion**

The rate of OHT (IOP ≥25 mmHg or increase ≥10 mmHg compared with baseline IOP) in our case series was 28.5% and the use of pressure-lowering eye drops was required in 31% of cases. These values are comparable to those described in pivotal studies and in real-life clinical practice.

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**Table 2. Time of the First Increase in Intraocular Pressure in Responding Patients**

<table>
<thead>
<tr>
<th>DEX Implant Injection Number</th>
<th>Total Number of DEX Implants (n)</th>
<th>IOP ≥25 mmHg, n = 73 (%)</th>
<th>Increase ≥6 mmHg, n = 183 (%)</th>
<th>Increase &gt;15 mmHg, n = 38 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEX 1</td>
<td>421</td>
<td>48 (11.4)</td>
<td>134 (31.9)</td>
<td>27 (6.4)</td>
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<tr>
<td>DEX 2</td>
<td>242</td>
<td>11 (4.5)</td>
<td>26 (10.7)</td>
<td>6 (2.5)</td>
</tr>
<tr>
<td>DEX 3</td>
<td>137</td>
<td>9 (6.6)</td>
<td>13 (9.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>DEX 4</td>
<td>87</td>
<td>3 (3.4)</td>
<td>5 (5.7)</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>DEX 5</td>
<td>54</td>
<td>2 (3.7)</td>
<td>2 (3.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>DEX 6</td>
<td>34</td>
<td>0 (0)</td>
<td>2 (5.9)</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>DEX 7</td>
<td>15</td>
<td>0 (0)</td>
<td>1 (6.7)</td>
<td>0 (0)</td>
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</tbody>
</table>

**Fig. 4.** Mean IOP for “multi-injected eyes” (eyes which have been administered 4 or more Ozurdex implants) over the duration of follow-up (n = 86).

<table>
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<th>Follow-up (months)</th>
<th>(n=86)</th>
<th>(n=86)</th>
<th>(n=86)</th>
<th>(n=86)</th>
<th>(n=82)</th>
<th>(n=80)</th>
<th>(n=80)</th>
<th>(n=75)</th>
<th>(n=56)</th>
<th>(n=33)</th>
<th>(n=19)</th>
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<tr>
<td>M0</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
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<tr>
<td>M2</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
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<tr>
<td>M3</td>
<td>15</td>
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<td>15</td>
<td>15</td>
<td>15</td>
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<td>15</td>
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</tbody>
</table>

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DEX, dexamethasone.
The OHT was mostly transient and successfully controlled with topical treatment in 97% of eyes. The rate of filtration surgery in our study (0.7%), which in all cases was performed on glaucoma patients treated at baseline with dual or triple therapy, was also similar to the data in the literature (1%). Slow-release dexamethasone is generally speaking well tolerated. The associated pressure tolerance is better than for triamcinolone acetonide 4 mg (40% OHT) and fluocinolone acetonide 190 μg (pressure-lowering treatment used in 38% of cases at 3 years, but with more high responders with 18% with IOP >30 mmHg and 4.8% requiring filtration surgery).15

To our knowledge, this study is the first to demonstrate that early retreatment between the third and fourth month does not result in any increased risk of IOP elevation post-DEX-I injection.

Another original feature of this study is that it identifies the risk factors of OHT (IOP ≥25 mmHg or an increase of ≥10 mmHg compared with baseline) over the follow-up period. Bold and italic values denote statistical significance with P < 0.05.

*Lens status, vitreous status, filtering surgery, and OHT on inclusion were not analyzed in the multivariate analysis as they were found to be nonsignificant in the univariate analysis.
†Axial length was not analyzed in the multivariate analysis as there was too much missing data (data available for 46% of cases).

<table>
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<tr>
<th>Characteristics</th>
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<th>Multivariate Analysis</th>
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<td>Crud OR</td>
<td>95% CI</td>
<td>P</td>
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<tr>
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<td>3.20</td>
<td>1.10–9.33</td>
<td>0.033</td>
</tr>
<tr>
<td>&gt;25 mm</td>
<td>3.20</td>
<td>1.10–9.33</td>
<td>0.033</td>
</tr>
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</table>

Association between the clinical variables and the probability of OHT (IOP ≥25 mmHg or an increase of ≥10 mmHg compared with baseline IOP) over the follow-up period.
IOP, over the course of the follow-up period) secondary to intravitreal DEX-Is, in addition to the glaucoma already described in a number of studies.\textsuperscript{12,16,17}

A previously published review\textsuperscript{18} described the risk factors associated with IOP elevation secondary to triamcinolone intravitreal injection. The identified variables were younger age, uveitis, baseline IOP $\geq 15$ mmHg, preexisting glaucoma, and a history of OHT with previous IVT steroid treatment.

In this study, regarding the demographic data, male patients and younger patients were the most at risk of developing OHT after Ozurdex implants.

Others studies have reported an association between OHT after intravitreal triamcinolone and younger age.\textsuperscript{18–20} Sex as a risk factor for IOP elevation after triamcinolone injection has also been described, but less consistently.\textsuperscript{18}

Regarding the ocular characteristics or ocular pathologies, preexisting glaucoma treated with dual or triple therapy, myopia with axial length of $>25$ mm, RVO and uveitis were associated with an increased risk of OHT after DEX-Is.

Ocular hypertension constitutes a well-known risk factor for RVO.\textsuperscript{21} In patient with uveitis, it is possible that the concomitant administration of topical and systemic corticosteroids could aggravate steroid-induced OHT. Furthermore, OHT is a complication of uveitis. In cases of intense inflammation, protein and inflammatory cell deposits build up in the trabecular meshwork hindering the outflow of the aqueous humor (trabeculitis), which in turn can lead to an increase in IOP.\textsuperscript{22}

Type 1 diabetes also seems to be an independent risk factor for OHT. There is however a possible bias in the present case series because of the much lower representation of patients with Type 1 diabetes (4\%) compared with Type 2 diabetes (96\%).

The analysis of this cohort also enables us to report that patients with DME seem to have a better pressure tolerance profile. Indeed, we found only 3\% of high responders and the percentage of OHT, as defined in this study, was particularly low in this group (17\%).

The percentage of OHT (17\%) in the DME group was also relatively low compared with the MEAD Study (27.7\%). This difference is no doubt due to methodological factors. The average follow-up period in the MEAD study was longer (36 months as opposed to 16.8 months in this study) with more visits in the pivotal study (monthly visits as opposed to a mean of 5 visits in the first year, 3.4 visits in the second year, and 3 visits in the third year for the DME group in our study). This means the MEAD study was statistically more likely to measure in increase in IOP. Furthermore, in this study, IOP measurements of $>20$ mmHg taken using air-puff tonometry were verified using applanation tonometry to detect any false positives. In these cases, the result obtained using Goldman applanation tonometry was the measurement retained, as this is the gold standard for measuring IOP.

Patients who developed elevated IOP after the first injection, often received prophylactic pressure-lowering therapy when subsequent injections were administered (first 3 months), which certainly also limited increases in IOP on retreatment. The same protocol was followed for the entire real-life cohort, regardless of the indication. Nonetheless, the DME group did show better pressure tolerance.

Maximum peak pressure in this study occurred at two months’ postintravitreal injection, a finding that concurs with the pivotal studies.\textsuperscript{4,5} However, we also observed earlier increases in IOP (IOP $\geq 25$ mmHg) as of day 8, in particular in patients with glaucoma, as well as later increases up to the third month.

Intraocular pressure should therefore be included in quarterly monitoring protocols, in particular in predisposed patients.

The incidence of OHT does not seem to increase with repeat DEX-I. In fact, the rate of OHT was artificially reduced as further DEX-Is were administered, because patients with OHT secondary to an DEX-I were either not retreated or given preventive IOP-lowering treatment for subsequent DEX-I.

The hypertension resulting from intravitreal DEX-Is is mostly successfully managed with IOP-lowering eye drops (97\% of cases in our series), and this medical management is not compromised by repeat DEX-I. It is therefore difficult to conclusively demonstrate the existence or not of a cumulative effect. Recently, Reid et al\textsuperscript{16} and Bakri et al\textsuperscript{23} concluded that repeat Ozurdex injections have no cumulative effect on IOP.

For the vast majority of patients who responded to intravitreal dexamethasone, the increase in pressure occurred at the first or second DEX-I (87\% of responding patients with an increase in IOP $\geq 6$ mmHg and 81\% of patients with IOP $\geq 25$ mmHg were diagnosed at the first or second injection). These data correspond to the findings of the MEAD study\textsuperscript{24} (79\% of patients with an increase in IOP $\geq 10$ mmHg were diagnosed at the first or second DEX-I). There was however 13\% of “late responders” in whom the first increase in IOP occurred after the third DEX-I or later. These “late responders” all presented with one of the aforementioned risk factors for IOP elevation.

These late responses are also observed when using fluocinolone acetonide 190 $\mu$g\textsuperscript{15} as 30\% of IOP-lowering therapies are required as of the 12th month of follow-up.

The reasons for these late responses are still poorly understood, but these findings emphasize the importance
of monitoring IOP in patients who receive multiple injections, especially if they present any of the risk factors for OHT.

In cases of bilateral injections, the IOP elevation observed in the first eye seems to be a good indicator of the expected pressure response in the fellow eye. In 84% of cases, the difference in the pressure increase between the 2 eyes, after the DEX-I injection, was less than 5 mmHg. Nonetheless, this means it is important to remain vigilant regarding the other 16%. Furthermore, 20% of patients presented unilateral OHT. To our knowledge, this is the first time this information has been reported in the literature and the reasons for this finding are not yet clear. The location of the implant in the vitreous and its proximity to the ciliary body, which vary from one injection to another, may also require consideration.

This study has limitations. Owing to its retrospective nature, the follow-up was relatively irregular, which means transient spikes in IOP might have been missed and the incidence of OHT therefore underestimated. Furthermore, the criteria for initiating IOP-lowering treatment were not predefined and were left to the discretion of the treating clinicians.

This study does however provide a better understanding of the predictive factors for pressure elevation and better defines the profiles of patients at risk of OHT after Ozurdex injections. In these at-risk patients, the use of Ozurdex must be justified and be subject to close monitoring.

Key words: adverse effects, corticosteroid, dexamethasone implant, intraocular pressure, ocular hypertension, ozurdex, risk factors.

References