Effectiveness and safety of dexamethasone implants for postsurgical macular oedema including Irvine–Gass syndrome: the EPISODIC-2 study

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ABSTRACT

Aim To assess the effectiveness of intravitreal dexamethasone implants for treating postsurgical macular oedema (PSMO) including Irvine–Gass syndrome and determining the predictive factors of treatment response.

Methods Descriptive, observational, retrospective, consecutive, uncontrolled, multicentre, national case series. One hundred patients were included between April 2011 and June 2014, with a minimum of 1-year follow-up. Patients received dexamethasone implant 0.7 mg at baseline. Clinical characteristics, best-corrected visual acuity (BCVA), central subfield macular thickness (CSMT) and intraocular pressure were measured at each visit. The main outcome measure was the change in BCVA (Early Treatment of Diabetic Retinopathy Study (ETDRS) letters): L. An analysis of predictive factors of treatment response is also provided.

Results Mean improvement in BCVA was 9.6 (±10.6) L at month 6 and 10.3 (±10.7) L at month 12 (p<0.001). The proportion of eyes with gains in BCVA of 15 or more letters was 32.5% and 37.5% at months 6 and 12, respectively. The mean reduction in CSMT was 135.2 and 160.9 μm at months 6 and 12, respectively (p<0.001). Thirty-seven per cent of patients did not need a second injection after the first injection during follow-up. The presence of at least one PSMO risk factor decreases the probability of a gain in visual acuity (VA) ≥10 L (p=0.006). Initial VA ≤50 L at baseline and non-naïve status decrease the probability of having only one injection during follow-up (p=0.044).

Conclusions The significant gain in BCVA from baseline achieved at month 6 was maintained at month 12 after intravitreal injection of dexamethasone implant. Naïve status seems to be a good predictive factor of treatment response.

INTRODUCTION

Postsurgical macular oedema (PSMO) is the main cause of visual loss after ophthalmic surgery. Irvine–Gass (IG) syndrome was initially clinically described by Irvine,1 and then angiographically characterised by Gass and Norton.2 Maumenee was the first to call it the Irvine–Gass syndrome. Incidence of IG syndrome is extremely variable and mainly depends on the series and also on the definition used. Clinical macular oedema (MO), with visual loss and metamorphopsia, occurs in 0.1%–2% of cases after uncomplicated modern cataract surgery.3 4 Spectral-domain optical coherence tomography (SD-OCT) MO occurs in 3.1%–41% of cases,5 6 and angiographic MO occurs in 0.1%–6% with visual loss and in 20%–30% without visual loss.4

With improvements in cataract surgery, notably the considerable reduction in the size of the incisions required during phacoemulsification, the incidence of clinically cystoid MO (CMO) significantly decreased, with peak incidence occurring on average 6 weeks after surgery.7 The most likely physiopathological hypothesis is that there is an inflammatory response instigated by the inflammatory mediators released during and after surgical procedures, causing alterations to the blood–retinal barrier. Many risk factors8–9 have been identified, such as posterior capsule rupture and vitreous loss, as well as the use of iris retractors, the presence of an epiretinal membrane, a vein occlusion, a history of uveitis or diabetes and the use of prostaglandin eye-drops.

In the last 20 years, no randomised studies have been conducted to establish the best therapeutic options. The most common first-line treatment is a combination of oral acetazolamide, used off-label, and the topical administration of non-steroidal anti-inflammatory drugs (NSAIDs). The approved indication for the latter is postoperative inflammation and not specifically postoperative MO. Second-line treatments include a range of therapies, also used off-label: intravitreal injections of steroids such as triamcinolone or dexamethasone implants,10–15 or intravitreal injections of antivascular endothelial growth factor (VEGF),16 17 or subcutaneous injections of interferon α-2a.18

The dexamethasone implant is a biodegradable intravitreal implant which delivers 700 μg of the corticosteroid dexamethasone into the vitreous and the retina. The implant has been approved for the treatment of MO, secondary to retinal vein occlusion,19 and for posterior inflammation such as non-infectious posterior uveitis.20 The use of dexamethasone intravitreal implant in PSMO including IG syndrome has already been studied in the pilot study EPISODIC,21 which is the largest published series using dexamethasone implant for that indication. This study shows a significant gain in visual acuity (VA) in 50 patients with a minimum follow-up of 6 months. It has also been used to treat 27 patients with IG syndrome in

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the phase II study on uveitis. Unfortunately, those patients with IG syndrome were mixed in with the patients with uveitis.\textsuperscript{15}

The objective of the present study was to confirm and complete our initial results obtained in the pilot study,\textsuperscript{21} this time with a larger sample of patients, with longer follow-up, in order to assess the anatomical and functional Effectiveness, as well as the Safety Of Dexamethasone implants (Ozurdex) in treating PSMO including Irvine–Gass syndrome (EpISODiC study 2). Specifically, we wanted to evaluate the change in best-corrected VA (BCVA) at 6 months (the primary outcome measure) and at 12 months; the proportion of eyes that gained 15 letters or more in Early Treatment of Diabetic Retinopathy Study (ETDRS) BCVA and the mean changes in central subfield macular thickness (CSMT) from baseline. A complementary analysis of the predictive factors of treatment response is also provided.

\textbf{MATERIALS AND METHODS}

A descriptive, observational, retrospective, consecutive, uncontrolled, multicentre case series was conducted in France from April 2011 to June 2014.

All patients received clear, detailed prior information on the treatment and on the expected risks and benefits. As the data were collected retrospectively and patients’ management was not modified, according to the French law (n°2004-806, 9 August 2004), this study did not require the research ethics committee’s approval. It was conducted in accordance with the law on data protection (n°2004-801, 6 August 2004).

All consecutive adult patients presenting clinical or subclinical PSMO including IG syndrome, treated with intravitreal injections of dexamethasone implant of 0.7 mg and followed up for at least 1 year were included in the study. All the patients were symptomatic, and the diagnosis was established with a precise fundus examination with indirect ophtalmoscopy and an OCT. In case of any doubt on OCT, the diagnosis was confirmed with fluorescein angiography. Patients initially included in the pilot study, who had a minimum follow-up of 1 year, were also included.

The inclusion and exclusion criteria used in the pilot study were maintained for this new series for the purposes of using the same methodology.

The patients were either naïve or non-naïve. All the previous treatments administered to each patient were identified.

Patients treated with oral corticosteroids, patients matching any of the contraindications for the dexamethasone intravitreal implant set out in the June 2013 marketing approval and patients with uncontrolled diabetes with glycosylated haemoglobin over 13% were excluded.\textsuperscript{15} Low baseline VA, anatomical OCT macular changes due to oedema persistence and a long duration of MO did not constitute exclusion criteria.

Each patient underwent a standardised examination on the first visit, and at each monthly follow-up visit, with measurement of BCVA in ETDRS letters (L), air-puff or applanation tonometer to measure intraocular pressure (IOP), ophtalmoscopy and SD-OCT to measure CSMT (thickness of a circular area of 1 mm, concentric to the foveal centre). Patients who received more than one injection underwent the same follow-up, and the same clinical and OCT data were collected.

Date and type of surgery, date of PSMO occurrence, eye-drops treatment, presence of PSMO risk factors, accurate history of PSMO treatment, with the type of treatment, duration and the number of other intra-ocular drugs injections were collected at baseline.

In case of MO recurrence during follow-up, the decision was made to administer an additional injection of dexamethasone implant, unless there were any contraindications for the patient in question. If any of the contraindications set out in the June 2013 marketing approval were found, the patients were excluded from the series. Re-treatment was performed in the event of recurrence of MO during follow-up. The time lapse between injections was clearly identified, as well as the number of injections administered during the follow-up period.

The main objective of our study was to assess the benefit of the dexamethasone intravitreal implant in treating PSMO including IG syndrome, with regular visits over a 1-year follow-up period, by measuring BCVA in L. The benefit of this treatment was also evaluated by measuring CSMT. In this new case series, we also wanted to evaluate the predictive factors of treatment response, and notably, to determine whether early treatment with dexamethasone intravitreal implant after PSMO diagnosis provides a better response. We then assessed the implant’s tolerance, measuring both local tolerance in terms of IOP iatrogenic retinal detachment or exogenous endophthalmitis, as well as overall tolerance. Then, we analysed the outcomes for patients with a minimum follow-up of 2 years.

\textbf{Statistical methods}

We used absolute and relative frequencies, and mean and SD, to describe categorical variables and quantitative variables, respectively.

Linear mixed effects models were used to estimate BCVA, CMST and IOP over time. In these models, individual trends were allowed to vary randomly and to deviate from the group average, according to within-individual and between-individual variances. This method also adjusted for the within-subject correlation of the repeated observations over time, and for the inclusion of patients with a varying number of measurements. BCVA was expressed using the absolute measured value or as the change (ie, gain) from the baseline value. Estimates at each time point were given with their 95\% CI.

In order to study factors associated with functional effectiveness, we used univariate and multivariate mixed effects logistic regression. Functional effectiveness was defined as a BCVA gain of ≥10 letters. Again, this method takes into account the fact that for each patient there were a number of potentially correlated BCVA measurements available from the follow-up period. The results are expressed as crude and adjusted OR, with their 95\% CI. OR of >1 indicated an increase in the probability of functional effectiveness.

The factors associated with recurrence after the first injection during the first year of follow-up were assessed using logistic regression. Recurrence was defined as more than one injection in the first year of follow-up. The results were reported as crude and adjusted OR, with their 95\% CI. OR of >1 indicated an increase in the probability of recurrence.

The R software program was used for all analyses, and for each test the 0.05 significance level was used.

\textbf{RESULTS}

This retrospective study was conducted in 12 centres located in mainland France (see online supplementary appendix 1).

One hundred consecutive patients were included between April 2011 and June 2014, with a minimum follow-up period of 1 year. The population characteristics are shown in table 1.

The mean age was 70.2 years (ranging from 20.9 to 100.4 years). Nine patients were under 55 years; 20 were between 55 and 65 years; 15 were between 65 and 75 years; 20 were between 75 and 85 years; and 34 were over 85 years.

The primary outcome measure was a BCVA gain of ≥10 letters, as measured from baseline. At 6 months, the proportion of eyes that gained 15 letters or more was 33.7\% (95\% CI 27.5–40.4\%). At 12 months, the proportion of eyes that gained 15 letters or more was 33.7\% (95\% CI 27.5–40.4\%).
In terms of the cause of MO, 58% were secondary to phacoemulsification cataract surgery (IG syndrome) and 42% secondary to other kinds of surgery (14% secondary to epiretinal membrane peeling, 9% secondary to combined cataract surgery and membrane peeling, 8% secondary to vitrectomy for retinal detachment and 11% after other surgeries), such as vitrectomy for intravitreal haemorrhage, capsulotomy neodymium-doped yttrium aluminium garnet or corneal graft. There was no significant difference between these two groups at diagnosis in terms of age (p=0.21), gender (p=0.54), mean delay between diagnosis and first dexamethasone intravitreal implant injection (p=0.89), mean follow-up (p=0.50), history of other treatments before the first injection (p=0.40), mean initial VA (p=0.34) and mean initial CSMT (p=0.66). For 37% of patients, initial VA was ≤50 L.

Concerning the PSMO risk factors, 15% of patients have had a complicated cataract surgery with capsular rupture, 4% a history of uveitis (with no other sign of inflammation), 2% had a history of RV and 4% were treated with prostaglandin eye-drops for glaucoma. Twenty-two per cent of patients had diabetes which was under control, 22% had high blood pressure and 34% had an epiretinal membrane (ERM). Sixteen patients were treated with monotherapy for glaucoma.

Concerning previous treatment, 15% of the patients were naïve. Of the remaining patients, 46% had been treated with topical NSAIDs and oral acetazolamide, 19% of patients had received the same treatment associated with intravitreal injection or subconjunctival injection of triamcinolone, 15% had the same treatment associated with intravitreal injection of anti-VEGF and 5% of patients had received at least three different treatments before their first intravitreal injection of dexamethasone implant. Out of all these patients, 8% required ERM peeling before the first injection.

The mean time from surgery to the diagnosis of PSMO was 4.8 (±7.1) months with a median time of 2 months. The mean time from the PSMO diagnosis to the first intravitreal injection of dexamethasone intravitreal implant was 3.8 (±5.2) months.

Concerning the entire population, the mean follow-up was 19.4 (±9.0) months, with a median follow-up of 16.4 months, with a range of 12.1–47.4 months. Twenty-five per cent of the patients had a minimum follow-up of 2 years.

During the first year of follow-up, 172 injections were administered to 100 patients. The mean number of injections was 1.77 during the first year. The average time to re-treatment was 5.9 months (ranging from 3.01 to 22.9 months), with a median time of 4.8 months. Thirty-seven per cent (37/100) of the patients needed only one injection during the first year and were considered cured (no recurrence with more than 1 year of follow-up). Thus, more than half of the patients did present a recurrence of MO after the first injection.

Dexamethasone intravitreal implant injection to treat PSMO including IG syndrome produced statistically significant improvements in BCVA (SD) at both month 6 and month 12. The mean initial VA was 57.1 (±16.6) L; the mean gain in VA was 9.6 (±10.6) L at month 6 and 10.3 (±10.7) L at month 12, with a mean VA of 66.7 (±18.3) L and 67.4 (±14.3) L at month 6 and month 12, respectively (figure 1) (p<0.001).

In the subgroup ‘IG’, initial mean BCVA was 38.5 (±15.6) L versus 54.8 (±17.8) L in the subgroup ‘PSMO excluding IG’ (p=0.34). In the subgroup ‘IG’, the mean BCVA was 69.6 (±16.8) L at month 6 and 71.0 (±12.0) L at month 12, respectively, versus mean BCVA of 61.1 (±19.5) L and 62.8 (±15.3) L, respectively in the subgroup ‘PSMO excluding IG’, which is significant (p=0.0035) (figure 1). The mean number of injections

### Table 1 Baseline patient characteristics

| Characteristic                                      | Number | Percentage |
|-----------------------------------------------------|--------|------------|
| Mean age (range)                                    | 70.2   | (20.9–100.4) |
| Sex                                                  |        |            |
| Male                                                | 58     | 58         |
| Female                                              | 42     | 42         |
| Laterality                                          |        |            |
| Right                                               | 47     | 47         |
| Left                                                | 53     | 53         |
| Type of surgery                                     |        |            |
| Phacoemulsification                                  | 58     | 58         |
| ERM peel                                            | 14     | 14         |
| Combined phacoemulsification—ERM peel               | 9      | 9          |
| Vitrectomy for retinal detachment                    | 8      | 8          |
| Other surgeries                                     | 11     | 11         |
| Initial VA                                          |        |            |
| ≤50 L                                                | 37     | 37         |
| >50 L                                               | 63     | 63         |
| Postsurgical macular oedema risk factors             |        |            |
| Capsular rupture                                    | 15     | 15         |
| History of uveitis                                  | 4      | 4          |
| History of retinal vein occlusion                   | 2      | 2          |
| Use of prostaglandin eye-drops                      | 4      | 4          |
| Blood pressure                                      | 22     | 22         |
| Diabetes                                            | 22     | 22         |
| ERM                                                  | 34     | 34         |
| Previous treatment                                  |        |            |
| Naïve patients                                       | 14     | 14         |
| Acetazolamide+NSAIDs only                           | 46     | 46         |
| Acetazolamide+NSAIDs only+triamcinolone injection   | 19     | 19         |
| Acetazolamide+NSAIDs only+anti-VEGF injection       | 15     | 15         |
| More than three treatments                           | 6      | 6          |
| ERM peeling (in association with other treatments)   | 8      | 8          |
| Antiglaucoma treatment                              |        |            |
| No treatment                                        | 83     | 83         |
| Treatment                                           | 16     | 16         |
| History of filtering surgery                        | 1      | 1          |
| Mean time from diagnosis, in months (minimum to maximum) | 4.8 (0.3–40.2) |
| Initial mean BCVA in letters (SD)                   | 56.9 (0–85) | ±16.6 |
| Initial mean CSMT, in μm (minimum to maximum) (range) | 522.9 (234–828) | ±132.5 |
| Mean time between diagnosis and first dexamethasone implant injection, in months (range) | 3.8 (0.9–23.2) | 5.2 |

BCVA, best-corrected visual acuity; CSMT, central subfield macular thickness; ERM, epiretinal membrane; L, Early Treatment of Diabetic Retinopathy Study (ETDRS) letters; NSAIDs, non-steroidal anti-inflammatory drugs; VA, visual acuity; VEGF, vascular endothelial growth factor.
during the first year of follow-up was nevertheless similar between these two groups, with a mean of 1.7 injections in the subgroup ‘IG’ and 1.8 injections in the other group.

The percentage of patients with an increase of more than 5, 10 and 15 letters was also assessed over the course of the follow-up period. The proportion of eyes that gained 5 letters or more was 76.2% at month 6 and 75.0% at month 12; the proportion of eyes that gained 10 letters or more was 53.8% at month 6 and 55.4% at month 12; and the proportion with a gain of 15 letters or more was 32.5% at month 6 and 37.5% at month 12 (figure 2).

Anatomical effectiveness was assessed by measuring mean CSMT using SD-OCT. Initial mean CSMT (SD) was 522.9 (±132.5) μm. At month 6, mean CSMT was 387.7 (±150.3) μm, corresponding to a reduction of 135.2 μm (p<0.001), compared with baseline. At month 12, mean CSMT was 362.0 (±118.3) μm, corresponding to a reduction of 160.9 μm (p<0.001) (figure 3).

In the subgroup ‘IG’, the main CSMT was 372.0 (±140.6) μm at month 6 and 342.7 (±120.7) μm at month 12, versus mean CSMT of 406.4 (±161.9) μm and 388 (±113.1) μm, respectively in the subgroup ‘PSMO excluding IG’, which is also significant (p=0.027) (figure 3).

The tolerance, primarily local tolerance, of the dexamethasone implant was then assessed by measuring mean IOP. Before the first injection, mean IOP was 13.4 (±3.9) mm Hg. At month 1, mean IOP was 15.5 (±6.0) mm Hg, which is not significant compared with baseline (p=0.134). After this first month, mean IOP observed was similar with a mean value of 14.2 (±3.1) mm Hg at month 2 (p=0.207), 13.4 (±4.2) mm Hg at month 6 (p=0.63) and 14.0 (±4.7) mm Hg at month 12 (p=0.214) (figure 4).

During the first year of follow-up, 19.2% of patients have had IOP of over 25 mm Hg, and 21% of patients needed a hypotensive treatment. Concerning the management of this complication, 25% of the patients needed a monotherapy, 60% needed a bitherapy and 15% a tritherapy. About 33.4% of patients with history of glaucoma have had IOP ≥25 mm Hg versus 16.7% of patients with no history of glaucoma (p=0.157). No filtering surgery was required.

Concerning other ocular adverse events, three patients have had intravitreal haemorrhage, two patients presented an anterior chamber migration of the implant (history of capsular rupture) and one patient presented a retinal detachment after the second injection. No systemic adverse events have been identified during the 1-year follow-up.

We also analysed the functional and anatomical effectiveness of dexamethasone implants in the subgroup of patients with 2 years of follow-up. Of the 100 patients initially included, 25 patients had a minimum of 2 years’ follow-up. During the second year of follow-up, 58 injections were administered. The mean number of injections per patient was 1.657 during the second year. Only one injection was needed by 57.1% of these patients during the second year of follow-up. Dexamethasone intravitreal implant injection in patients with PSMO produced statistically significant improvements in BCVA (SD) at both month 18 and month 24, with a mean gain in VA of 10.0 (±14.9) L at month 18 and 5.4 (±16.6) L at month 24, with a mean VA of 66.9 (±18.3) L and 62.3 (±14.3) L, respectively, at month 18 and month 24, compared with baseline (p<0.001). The percentage of patients with an increase of more than 5, 10 and 15 letters was also assessed over the course of the second year of follow-up. The mean number of injections per patient was 1.657 during the second year. Only one injection was needed by 57.1% of these patients during the second year of follow-up.
the follow-up period. The proportion of eyes that gained 5 letters or more was 62.2% at month 18 and 58.3% at month 24; the proportion of eyes that gained 10 letters or more was 50.0% at month 18 and 50.0% at month 24; and the proportion with a gain of 15 letters or more was 35.3% at month 18 and 27.8% at month 24 (figure 2). Concerning CSMT, the difference is still significant; at month 18, mean CSMT was 346.9 (±115.7) μm, corresponding to a reduction of 176 μm (p<0.001), compared with baseline. At month 24, mean CSMT was 340.2 (±116.7) μm, corresponding to a reduction of 182.7 μm (p<0.001). During 2 years or more of follow-up, 100% of these 25 patients presented anatomical effectiveness defined as a minimum decrease of 50 μm in CSMT. Concerning local tolerance, mean IOP was 13.5 (±4.3) at month 18 and 13.3 (±4.1) at month 24. IOP of ≥25 mm Hg was presented by 6.2% of patients. No filtering surgery was required.

Figure 5 represents the trend after the first injection. One hundred patients received a first intravitreal injection at baseline. Of these patients, 37 did not need a second injection during the year after the first injection and were considered as cured. Sixty-three patients needed a second injection, with a mean time to re-treatment of 7.02 months. Concerning these 63 patients, 4 patients did not need a third injection during the year after the second injection and were considered as cured. Finally, we analysed independent predictive factor of treatment response. First of all, we wanted to identify predictive factors of functional effectiveness and then analyse the predictive risk factors for anatomical and functional recurrence after the first injection, during the first year of follow-up.

Different potential predictive risk factors were analysed, such as type of surgery responsible for the PSMO, initial VA ≤50 L or >50 L (20/100 in Snellen equivalents), mean time ≤3 months or >3 months from diagnosis to the first intravitreal injection of dexamethasone intravitreal implant, class of age of patients, naïve or non-naïve patients and presence of at least one PSMO risk factor: presence of capsular rupture, history of uveitis or retinal vein occlusion, use of prostaglandin eye-drops, history of diabetes, high blood pressure or presence of ERM. A significant difference in functional effectiveness was defined as a mean gain of ≥10 L during follow-up. In the univariate analysis, the presence of a PSMO risk factor at diagnosis is a predictive factor of treatment response with a better functional effectiveness in the subgroup with no PSMO risk factors compared with...
the group with at least one PSMO risk factor (p=0.021). Indeed, the presence of at least one PSMO risk factor decreases by 77% the probability of a gain in VA of ≥10 L. Initial VA was also a predictive factor. Indeed, initial VA of >50 L decreases the probability of a visual gain of ≥10 L (p=0.002). Mean time to the first injection after diagnosis (p=0.932), age of patients (p=0.316), history of other general or local treatments for PSMO prior to dexamethasone intravitreal implant (p=0.511) and the type of surgery responsible for PSMO (p=0.231) seem not to be predictive factors of functional effectiveness (table 2).

In the multivariate analysis, the presence of at least one PSMO risk factor decreases by 69% the probability of a gain in VA of ≥10 L (p=0.006). Initial VA of >50 L decreases by 77% the probability of a gain in VA of ≥10 L (p<0.001). The aetiology ‘post phacoemulsification’ multiplies by 2.4 the probability of having a gain in VA of ≥10 L (p=0.045) compared with the aetiology ‘other surgery’.

Concerning the predictive risk factors for recurrence and thus for requiring a further injection after the first injection during the first year of follow-up, in the univariate analysis, initial VA of >50 L at baseline multiplies by 2.4 the probability of needing only one dexamethasone implant injection, that is to say no recurrence (p=0.050). Type of surgery (p=0.332), mean time to first injection after diagnosis (p=0.978), age of patients (p=0.665), history of other general or local treatments for PSMO prior to dexamethasone implant (p=0.162) and the presence of at least one PSMO risk factor (p=0.409) seem not to be predictive factors of recurrence (table 3).

In the multivariate analysis, initial VA of >50 L at baseline multiplies by 3 the probability of having only one injection during follow-up (p=0.029), and non-naïve status decreases by 76% the probability of having only one injection, that is, naïve status multiplies by 4.1 the probability of needing only one injection during follow-up (p=0.044).

**DISCUSSION**

PSMO is a genuine therapeutic challenge, because although it can heal spontaneously, it can also persist, causing permanent damage to the macular and decreasing VA. Today, there is no consensus on the best care management to offer patients; so,

**Table 2** Univariate analysis of predictive factors of functional effectiveness defined as a mean gain of 10 L

| Variable/value                     | OR     | 95% CI          | p Value |
|------------------------------------|--------|-----------------|---------|
| Type of surgery                    |        |                 |         |
| Other surgery                      |        |                 |         |
| Phacoemulsification                | 1.847  | 0.792 to 4.306  | 0.156   |
| Initial VA                         |        |                 |         |
| ≤50 L                              | 0.286  | 0.128 to 0.641  | 0.002   |
| >50 L                              |        |                 |         |
| Time between diagnosis and first injection (months) |        |                 |         |
| ≤3                                 | 0.970  | 0.484 to 1.944  | 0.932   |
| >3                                 |        |                 |         |
| Age group (years)                  |        |                 |         |
| ≤55                                | 1.902  | 0.482 to 7.511  | 0.359   |
| 55–65                              | 1.433  | 0.404 to 5.082  | 0.577   |
| ≥75                                | 1.022  | 0.290 to 3.602  | 0.974   |
| Naïve patients                     |        |                 |         |
| Yes                                | 1.370  | 0.536 to 3.499  | 0.511   |
| No                                 |        |                 |         |
| PSMO risk factors                  |        |                 |         |
| No                                 | 0.343  | 0.170 to 0.683  | 0.021   |

L, Early Treatment of Diabetic Retinopathy Study (ETDRS) letters; PSMO, postsurgical macular oedema; VA, visual acuity.

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the treatment depends on individual physicians’ preferences and habits. In the event of capsular rupture with vitreous loss and presence of vitreous in the anterior segment, the safe and thorough evacuation of vitreous from the anterior chamber, sometimes associated with a posterior vitrectomy, is the first-line recommended treatment. First-line treatments often include oral acetazolamide associated with NSAIDs eye-drops, but the numerous adverse effects linked to acetazolamide, including renal colic, cramps, formication and asthenia mean that this is not always a suitable choice. Second-line treatments include a range of therapies used off-label. Before embarking on therapeutic intensification and the use of steroids or immunosuppressive drugs, it is vital that an angiography is carried out, at the very least, to eliminate differential diagnoses such as uveitis.

The intravitreal injection of anti-VEGF can be used to inhibit macular oedema; VA, visual acuity.

### Table 3

Univariate analysis of predictive risk factors of recurrence after the first injection

| Variable/value | OR   | 95% CI     | p Value |
|----------------|------|------------|---------|
| Type of surgery |      |            |         |
| Phacoemulsification | 1.552 | 0.638 to 3.775 | 0.332   |
| Other surgery |      |            |         |
| Initial VA |      |            |         |
| ≤50 L | 2.562 | 1.390 to 6.316 | 0.041   |
| >50 L |      |            |         |
| Time between diagnosis and first injection (months) |      |            |         |
| ≤3 | 0.998 | 0.427 to 2.288 | 0.978   |
| >3 |      |            |         |
| Age group (years) |      |            |         |
| ≤55 | 3.500 | 0.346 to 5.371 | 0.288   |
| 55–65 | 6.588 | 0.727 to 9.679 | 0.094   |
| 65–75 | 3.667 | 0.399 to 3.714 | 0.251   |
| ≥75 |      |            |         |
| Naïve patients |      |            |         |
| Yes | 0.453 | 0.149 to 1.374 | 0.162   |
| No |      |            |         |
| PSMO risk factors |      |            |         |
| Yes | 0.704 | 0.307 to 1.617 | 0.409   |
| No |      |            |         |

L, Early Treatment of Diabetic Retinopathy Study (ETDRS) letters; PSMO, postsurgical macular oedema; VA, visual acuity.
It is also interesting to note that the kind of surgery responsible for PSMO seems to be an important prognosis factor. Indeed, there is a significant difference in terms of functional and anatomical effectiveness between the two groups analysed, with a better response in the subgroup ‘IG’. These data have not been yet studied, and regarding our results it would appear that IG syndrome and other PSMO are two different identities. However, even if there is a significant difference in the functional effectiveness, there does not appear to be a difference between the number of injections needed. Indeed, in the subgroup of ‘IG’, patients needed a mean number of 2.3 injections during the mean follow-up of 19.0 months, compared with a mean number of 2.9 injections in the other group for a mean follow-up of 20.0 months (p=0.25). One can presume that in cases of vitrectomy for retinal detachment or ERM peeling, the presence of an underlying macular disease represented a poor prognosis factor of functional effectiveness; however, these data have not been yet analysed in the literature.

Regarding the predictive factors, we first analysed the predictive factors of good response to treatment defined as a gain of at least 10 L in BCVA during follow-up. Only the absence of PSMO risk factors at diagnosis proved to be a good predictor of functional effectiveness (p=0.041), while the patient’s age, type of surgery, initial VA, the naïve status and the time of first injection did not constitute predictive factors of good response to treatment, both in the univariate analysis and in the multivariate analysis. Concerning the predictive risk factors for recurrence after the first injection during the first year of follow-up, initial VA of >50 L at baseline was the only predictive factor associated with a lower risk of recurrence in the univariate analysis. In the multivariate analysis, initial VA of >50 L at baseline and naïve status were predictive factors associated with a lower risk of recurrence.

It should also be noted that very few adverse effects were reported during follow-up, with no cases of filtering surgery or iatrogenic retinal detachment. No systemic adverse events were observed.

The use of corticosteroids is not limited to dexamethasone implants. Several studies have analysed the benefit of intravitreal injections of triamcinolone from 2 to 4 mg for treating MO, secondary to ophthalmic surgery. Periocular corticosteroids have also been shown to be effective for pseudophakic CMO refractory to topical treatments. Sub-Tenon’s betamethasone has also shown benefits in IG treatment.

Finally, the present study shows significant functional and anatomical improvements as compared with baseline with a functional gain of more than two ETDRS lines over the follow-up period. Although some patients experienced a recurrence in CMO, BCVA and/or mean CSMT at the end of follow-up, these measurements were still better than those at baseline. The dexamethasone implant would therefore appear to be a safe and effective therapeutic option for PSMO including IG syndrome. The absence of PSMO risk factors at diagnosis seems to be a good predictive factor of treatment response.

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Competing interests VP-K—has sat on advisory boards and received lecture fees from Allergan, Bayer and Novartis; FM—investigator for trials sponsored by Novartis, Bayer and Alcon; has sat on advisory boards for Allergan and Bayer; received lecture fees from Allergan, Bayer and Novartis; CD—reports personal fees from Allergan, Alcon, Bayer and Novartis, outside the submitted work; JA—co-investigator for the trial sponsored by Novartis; has sat on advisory boards for Allergan and Bayer; received lecture fees from Allergan, Bayer and Novartis; SM—investigator for trials sponsored by Bayer and Novartis; VS—received consultant fees from Allergan, Bayer, Essilor and Novartis; SB—sat on advisory boards for Novartis, Bayer and Alcon; received lecture fees from Alcon, Allergan, Bayer, FCI, Novartis and Thèa; received lecture fees from Alcon, Allmera, Allergan, Bayer, FC, Novartis and Thèa; CD—sponsored for the trials sponsored by Novartis, Bausch&Lomb, Thèa and Alcon; has sat on advisory boards for Alcon, Alimera, Allergan, Bayer, FC, Novartis and Thèa; received lecture fees from Alcon, Alimera, Allergan, Bayer, Novartis and Thèa; VP-K—principal investigator for trials sponsored by Novartis, Bausch&Lomb, Thèa and Alcon; has sat on advisory boards for Alcon, Alimera, Allergan, Bayer, Bausch&Lomb, Novartis and Thèa; received lecture fees from Alcon, Alimera, Allergan, Bayer, Bausch&Lomb, Novartis and Thèa.

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