Ocriplasmin injection provides nonsurgical alternative for VMA release

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Prior to the development of intravitreal ocriplasmin injection (Jetrea, ThromboGenics, Inc.), the only options for treating patients with symptomatic vitreomacular adhesion (sVMA) were surgery or observation. Vitreomacular adhesion (VMA) can cause significant traction on the macula at the vitreomacular interface causing macular dysfunction and macular holes. Patients with sVMA frequently complain of blurred vision, distortion, decreased vision and central microscotomas. Ocriplasmin is the first FDA-approved pharmacologic agent used in the treatment of patients with sVMA that can induce the release of vitreomacular adhesion (VMA) without surgery.

...[A]s my colleagues and I have become more discerning with our patient selection based on the known positive predictive factors, our success rate has improved.

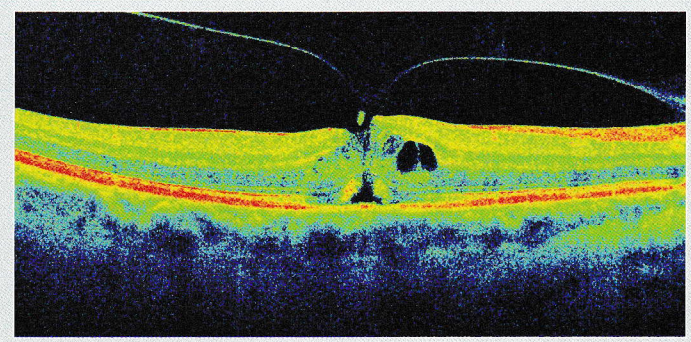
Patient selection

Appropriate patient selection is critical for achieving successful outcomes with ocriplasmin injection. Higher response rates and successful outcomes can be achieved by selecting patients with positive predictive factors identified in the Microplasmin for Intravitreous Injection-Traction Release without Surgical Treatment (MIVI-TRUST)

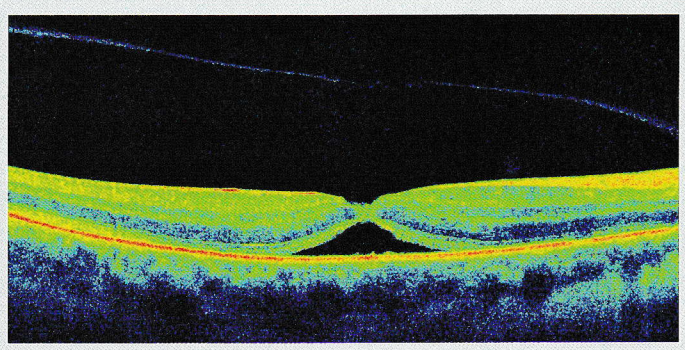
Case 1: 59-year-old male

The patient presented with a 1-month history of loss of vision in the right eye and visual acuity (VA) of 20/80. A preinjection OCT scan revealed a small full thickness macular hole measuring 220 µm with intraretinal cystic changes and obvious focal vitreomacular traction (VMT). At 1 week postinjection, the OCT scan showed that the macular hole had closed, the VMT released and the posterior hyaloid elevated above the macular, as well as the presence of subretinal fluid. The patient's VA improved to 20/40. At 3 months postinjection, the OCT showed almost complete normalization of foveal architecture, good foveal depression and good visualization of all four bands of outer retina. A very small residual amount of subretinal fluid remained.

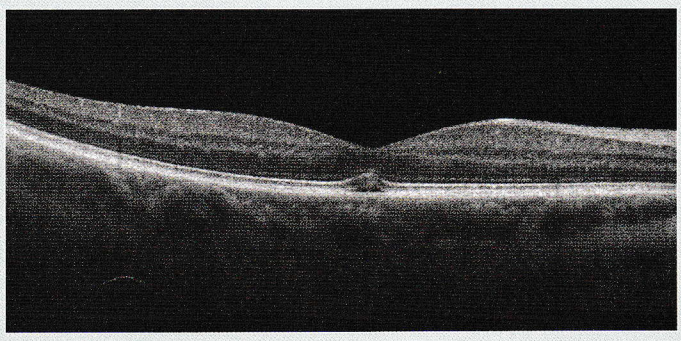
Preinjection



1 week



3 months

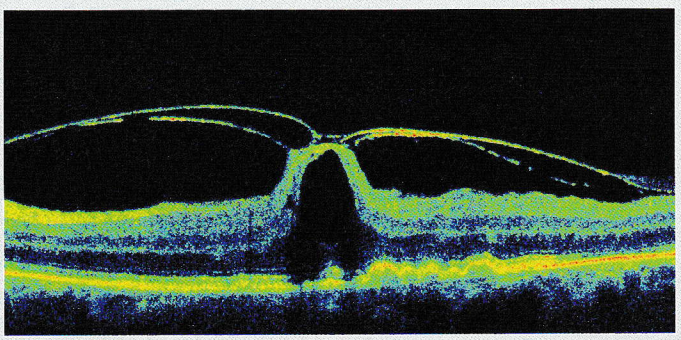


Source: Katz RS

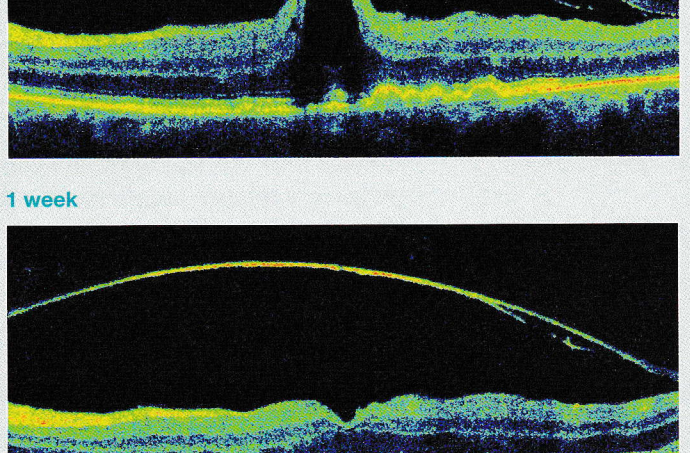
Case 2: 61-year-old male

The patient complained of distortion in the left eye with a visual acuity (VA) of 20/30 in the right eye and 20/60 in the left eye. The patient had a history of age-related macular degeneration and was being treated with Avastin (bevacizumab, Genentech) for wet macular degeneration in the right eye for 1 year. The patient's preinjection OCT scan shows a focal vitreomacular adhesion (VMA) less than 1,500 µm and an epiretinal membrane under the hyaloid. One week after injection, the patient's VA improved to 20/25, the VMA released and the foveal contour returned to almost normal. At 4 weeks postinjection, the patient's VA improved to 20/20, and the OCT scan revealed complete vitreous detachment of the macula with almost normal foveal architecture. There was also shallow drusenoid pigment epithelial detachment nasal to center of fovea.

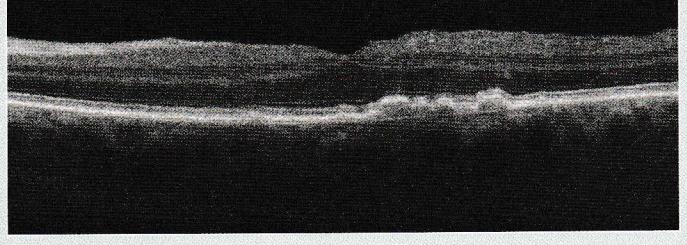
Preinjection



1 week



3 months



Source: Katz RS

phase 3 clinical trial.[1] These factors are: VMA of 1,500 µm or less, no epiretinal membrane (ERM) present, macular holes of 250 µm or less in diameter, patients with a phakic lens and patients 65 years of age or younger. The chance for success improves when more positive predictive factors are present.[1,2]

When treating patients with symptomatic VMA, it is important for surgeons to present all of the treatment options as well as the benefits, risks and success rates associated with each.

In a recent study, Singh and colleagues achieved a 50% success rate in patients with at least three positive predictive factors and a 75% success in patients with four positive predictive factors—no ERM, VMA of 1500 µm or less, phakic lens status and patients 65 years of age or younger.[2] In my experience, patients who respond poorly to ocriplasmin injection are patients aged 65 years or older and patients with significant ERMs and/or a VMA of 1,500 µm or larger. In addition, patients who have had cataract surgery and patients with large macular holes 400 µm or larger, also typically experience less successful outcomes with ocriplasmin injection. In my practice, we have treated 35 patients with ocriplasmin injection, and our success rate is approximately 40%. However, as my colleagues and I have become more discerning with our patient selection based on the known positive predictive factors, our success rate has improved. Of my last 20 patients with sVMA treated with ocriplasmin injection, 12 patients have had a successful result (60%), which I attribute to better patient selection using these positive predictive factors as a guide.

Successful outcomes

If a patient is going to respond to the injection, the release typically occurs within 1 week of injection. Approximately 80% of patients respond

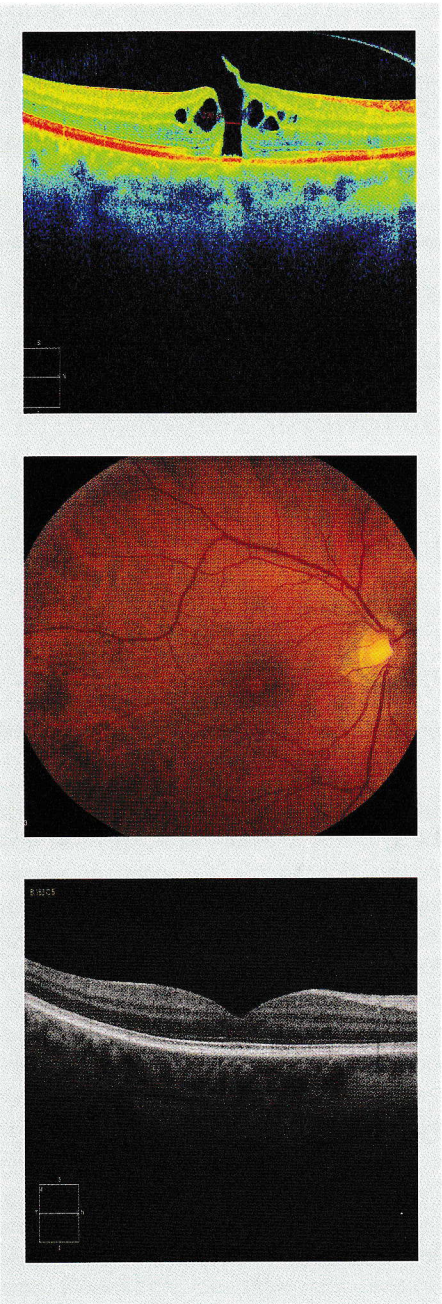


Figure 1. The patient, a 59-year-old male, presented with a 1-month history of loss of vision in the right eye and visual acuity (VA) of 20/80 (top). The patient had had no previous ocular surgeries and four positive predictive factors: aged 65 years or younger, a small macular hole of less than 250 µm, phakic status and no epiretinal membrane (middle). The patient's VMA released within 1 week, and VA improved to 20/40. At 3 months postinjection, the patient's VA was 20/25 (bottom).

Source: Katz RS

within 1 week, and the remainder of the responders will demonstrate release within 3 to 4 weeks of injection. After 1 month, it is unlikely that a patient will have a successful result with VMA release.

A successful outcome after using ocriplasmin injection is considered release of the VMA. However, patient satisfaction and elimination of the patient's symptoms are the ultimate goals of treatment. If the patient's symptoms have been eliminated and if surgery has been avoided, then a successful outcome has been achieved. In my practice, I treated a patient who had a macular hole with vitreomacular traction (VMT) with an ocriplasmin injection. The VMA released, but the patient's visual acuity (VA) worsened slightly, and the macular hole did not close, enlarged slightly and was accompanied by more perifoveal fluid.

If a patient is going to respond to the injection, the release typically occurs within 1 week of injection.

Technically, this procedure was a success, but realistically, it was a failure. The patient underwent pars plana vitrectomy with membrane and internal limiting membrane peel, and the macular hole closed and the patient's VA improved. The MIVI-TRUST trial demonstrated that a patient's final VA and outcome will not be adversely affected by ocriplasmin injection when pars plana vitrectomy is subsequently performed.

Macular holes

The International Vitreomacular Traction Study Group developed a unifying system for defining and classifying VMAs and macular holes. This study group developed on optical coherence tomography–based anatomic classification system to better characterize diseases of the vitreomacular interface. This system allows for more accurate categorization of VMA, VMT and macular holes based on strict OCT anatomic definitions. This classification can be used to determine whether a patient is a good candidate for ocriplasmin injection.[3]

The researchers classified macular holes into three categories: small macular holes of 250 µm or less, medium macular holes of 250 µm to 400 µm and large macular holes of 400 µm or larger. Based on this classification, the researchers determined that, when ocriplasmin injection is used, patients with small macular holes have a 60% chance for success; patients with medium macular holes have a 40% chance for success; and patients with large macular holes have a 0% chance for success (Figure 1).[3]

Patients with macular holes also can experience a delayed improvement in VA. My patients typically return 1 week after injection and, even if the macular hole is closed at that time, the patient's vision may not have improved. These patients frequently have expressed subjective improvement, and improvement in visual acuity generally occurs over the next several weeks or months, because there can be slow resolution of residual subretinal fluid and probable recovery of photoreceptor function.

Setting patient expectations

When treating patients with symptomatic VMA, it is important for surgeons to present all of the treatment options as well as the benefits, risks and success rates associated with each.

If ocriplasmin injection is chosen, then it is important for surgeons to emphasize that the success rate is approximately 40% to 50% based on the patient's

positive predictive risk factors. It is also important to emphasize that if the injection is unsuccessful, it will not have any detrimental impact on the success of future surgical options.[1]

Additionally, it is critical for surgeons to explain the symptoms and side effects that can occur immediately after the injection. These can be dramatic and alarming to patients if they have not been appropriately counseled. Immediate postoperative side effects can include a dramatic decrease in vision, blurred vision, photopsias, flashes and floaters, decreased contrast and dyschromatopsia. The severity of the flashing lights and floaters on the first postoperative evening can be particularly frightening for patients. However, these symptoms are usually transient and generally resolve within 1 week of injection.

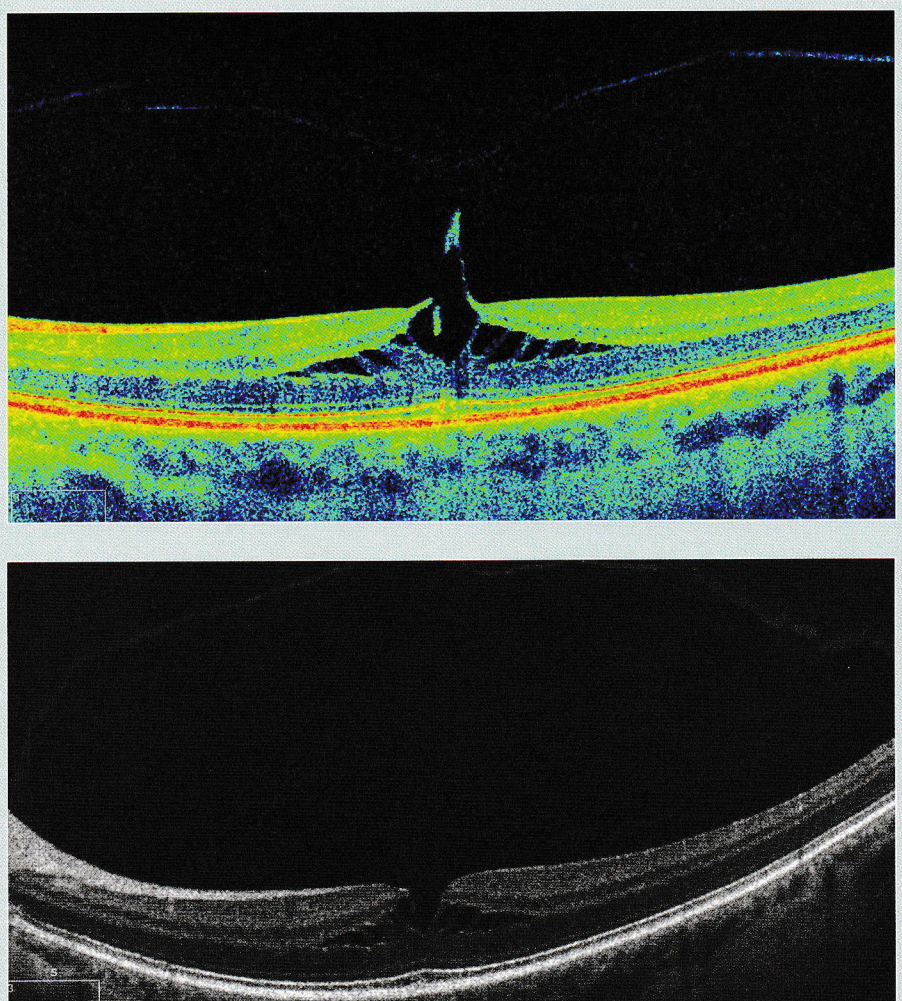


Figure 2. The patient, a 59-year-old moderately myopic female, complained of a "spot in center of vision in left eye" for 2 weeks. The patient's visual acuity (VA) was 20/25 OS. The baseline OCT scan (top) shows focal vitreomacular adhesion (VMA) with retinal elevation accompanied by lamellar hole and schisis cavities. In addition, there was mild disruption of the ellipsoid zone. The patient was observed monthly for 3 months without resolution of symptoms, and ocriplasmin injection was scheduled for the following week. On the day of the scheduled injection, preoperative OCT scans revealed complete release of vitreomacular traction with elevation of posterior hyaloid (bottom). There was a persistent lamellar defect with schisis cavity, but the OS ellipsoid zone under fovea was restored. The scheduled injection was cancelled, and the patient's symptoms resolved quickly. The patient's VA improved to 20/20 and the patient is asymptomatic. There was a persistent lamellar defect and schisis cavity, but the integrity of the ellipsoid zone under the fovea was restored.

Source: Katz RS

If ocriplasmin injection is chosen, then it is important for surgeons to emphasize that the success rate is approximately 40% to 50% based on the patient's positive predictive risk factors.

After ocriplasmin injection, patients often experience worsening of the VMT accompanied by increased subretinal fluid and outer segment (OS) ellipsoid zone loss. This OS ellipsoid zone loss is usually transient and resolves quickly without permanent sequelae.[2] However, Tibbetts and colleagues[4] reported a patient with persistent darkening of vision in dim illumination after ocriplasmin injection. According to the patient's OCT scans, the patient also demonstrated disruption of the ellipsoid layer and reduced electroretinogram amplitudes corresponding to the patient's symptoms of darkened vision. The researchers hypothesized that ocriplasmin injection may have a diffuse enzymatic effect on photoreceptors or the retinal pigment epithelium that is not limited to areas of vitreomacular traction.[4]

Administration

Ocriplasmin injection is fairly simple to administer. It is stored in a specialized freezer at -20°C. Before removing the medication from the freezer, the physician should perform an OCT scan and examine the patient to confirm that the VMA has not spontaneously released, because once the medication has been removed from the freezer, it cannot be refrozen. In my experience, I have occasionally seen the VMA release spontaneously between the last exam and the day of scheduled ocriplasmin injection (Figure 2, page 11). Postoperatively, I have the patient lie supine on his or her back for 20 to 25 minutes immediately after the injection and ask him or her to perform ocular movements, which should help disperse the medication and avoid autocatalysis.[5]

Ocriplasmin provides an option for patients with sVMA to potentially avoid surgery, and patients who respond to ocriplasmin injection achieve a successful outcome without the risks and postoperative inconvenience of vitrectomy or post-vitrectomy cataract surgery.

My overall experience using ocriplasmin injection has been excellent. By choosing appropriate patients, ophthalmologists can expect a success rate of approximately 50%. Ocriplasmin provides an option for patients with sVMA to potentially avoid surgery, and patients who respond to ocriplasmin injection achieve a successful outcome without the risks and postoperative inconvenience of vitrectomy or post-vitrectomy cataract surgery.

In summary, ocriplasmin injection is the first FDA-approved medication for the treatment of patients with sVMA, and it represents a new treatment option to be considered along with observation and pars plana vitrectomy. It is an office-based intravitreal procedure that can induce release of VMT in patients with sVMA. However, careful patient selection based on positive predictive risk factors and appropriate management of patient expectations are important. Counseling and discussion concerning immediate postoperative side effects, as well as risks, benefits and treatment alternatives, should occur before injection, and patients who choose to receive ocriplasmin injection should be followed closely postoperatively.

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In the next issue of The **Ocriplasmin** Experience:

- Physician experiences with ocriplasmin injection
- Case presentations
- Coverage from AAO 2014

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