CURRENT TREATMENT OPTIONS FOR VITREOMACULAR ADHESION AND MACULAR HOLE

With articles by
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SYMPTOMATIC VITREOMACULAR ADHESION (VMA) IS A CONDITION IN WHICH THE VITREOUS GEL ADHERES IN AN ABNORMALM  STRONG MANNER TO THE RETINA. VMA CAN LEAD TO VITREOMACULAR TRACTION (VMT) AND SUBSEQUENT LOSS OR DISTORTION OF VISUAL ACUITY. ANOMALOUS POSTERIOR VITREOUS DETACHMENT (PVD) IS LINKED TO SEVERAL RETINAL DISORDERS INCLUDING MACULAR PUCKER, MACULAR HOLE, AGE-RELATED MACULAR GENERATION (AMD), MACULAR EDEMA, AND RETINAL TEARS AND DETACHMENT.

THE INCIDENCE OF VMA HAS BEEN REPORTED TO BE AS HIGH AS 84% IN CASES OF MACULAR HOLE; 74% IN VMT; AND 56% IN IDIOPATHIC EPIMACULAR MEMBRANE.1 THE INCIDENCE OF VMA IN MACULAR EDEMA APPEARS TO DEPEND ON THE SEVERITY OF THE UNDERLYING CONDITION.2,3,10,11

CURRENTLY, PARAS PLANAR VITRECTOMY (PPV) IS USED TO SURGICALLY INDUCE PVD AND RELEASE THE TRACTION ON THE RETINA FOR SELECTED CASES. A VITRECTOMY PROCEDURE, HOWEVER, IS NOT WITHOUT RISK. COMPLICATIONS REPORTED WITH STANDARD PPV12-15 AND MORE RECENTLY WITH SMALL-GAUGE PPV16-20 INCLUDE RETINAL DETACHMENT, RETINAL TEARS, ENDOPTHALMITIS, AND POSTOPERATIVE CATARACT FORMATION. ADDITIONALLY, PPV MAY RESULT IN INCOMPLETE SEPARATION, AND IT MAY POTENTIALLY LEAVE A NIDUS FOR Vasoactive AND VASProliferative SUBSTANCES, OR IT MAY POTENTIALLY LEAVE A NIDUS FOR SPONTANEOUS OR INVASIVE PROCEDURES, PPV INTRODUCES TRAUMA TO THE VITREOUS AND SURROUNDING TISSUES.

DATA SHOW THAT NONSURGICAL INDUCTION OF PVD USING OCRIPLASMIN, A VITREOLYSIS AGENT, CAN OFFER THE BENEFITS OF SUCCESSFUL PVD WHILE ELIMINATING THE RISKS ASSOCIATED WITH A SURGICAL APPROACH. PHARMACOLOGIC VITREOLYSIS HAS THE FOLLOWING ADVANTAGES OVER PPV: IT INDUCES COMPLETE SEPARATION, CREATES A MORE PHYSIOLOGIC STATE OF THE VITREOMACULAR INTERFACE, PREVENTS THE DEVELOPMENT OF FIBROVASCULAR MEMBRANES, IS LESS TRAUMATIC TO THE RETINA, AND IS POTENTIALLY PROPHYLACTIC.1,11,12 ADDITIONALLY, PHARMACOLOGIC VITREOLYSIS OBVIATES THE COSTS ASSOCIATED WITH SURGERY AND ALLOWS EARLIER INTERVENTION, WHEREAS SURGERY IS RESERVED FOR MORE ADVANCED CASES. IN 2 PHASE 3 STUDIES, A SINGLE INJECTION OF OCRIPLASMIN WAS SHOWN TO BE SAFE AND EFFECTIVE FOR PVD INDUCTION,22,24 PROVIDING FURTHER EVIDENCE THAT PHARMACOLOGIC VITREOLYSIS WITH OCRIPLASMIN MAY PROVIDE A SAFE AND EFFECTIVE ALTERNATIVE TO PPV FOR INDUCING PVD.

RETINA SPECIALISTS AND OTHER OPHTHALMOLOGISTS MUST MASTER INSIGHTS ON THE PATHOGENESIS OF VMA, THE ROLE THAT VMA PLAYS IN VARIOUS RETINAL PATHOLOGIES, AND THE BENEFITS OF INDUCED PVD Vs ANOMALOUS PVD. MASTERY INCLUDES KNOWLEDGE OF THE CLINICAL IMPLICATIONS OF VMA AND THE RESULTS OF RECENT CLINICAL TRIALS ON BOTH SURGICAL AND PHARMACOLOGIC PVD INDUCTION, AN UNDERSTANDING OF VITREOLYSIS AGENTS AND THEIR DIFFERENCES, AND THE ABILITY TO IDENTIFY PATIENTS WHO MAY BENEFIT FROM PVD INDUCTION.


TARGET AUDIENCE

This certified CME activity is designed for retina specialists and general ophthalmologists involved in the management of patients with retinal disease.

LEARNING OBJECTIVES –

Upon completion of this activity, the participant should be able to:

- Describe the clinical implications of VMA and the results of recent clinical trials on both surgical and pharmacologic PVD induction, an understanding of vitreolysis agents and their differences, and the ability to identify patients who may benefit from PVD induction.

- Master insights on the pathogenesis of VMA, the role that VMA plays in various retinal pathologies, and the benefits of induced PVD vs anomalous PVD. Mastery includes knowledge of the clinical implications of VMA and the results of recent clinical trials on both surgical and pharmacologic PVD induction, an understanding of vitreolysis agents and their differences, and the ability to identify patients who may benefit from PVD induction.
CURRENT TREATMENT OPTIONS FOR VITREOMACULAR ADHESION AND MACULAR HOLE

- Identify the key anatomic elements of the vitreous and the areas of vitreomacular adhesion
- Understand the normal progressive anatomic changes that occur in the vitreous over time
- Differentiate the various vitreous disease states associated with VMA
- Understand the use of OCT imaging in VMA disease states
- Compare normal PVD vs anomalous PVD
- Discuss the mechanism of action of pharmacologic vitreolysis and delivery techniques
- Discuss recent safety and efficacy data of pharmacologic vitreolysis agents used in VMA treatment
- Participants should read the CME activity in its entirety.

METHOD OF INSTRUCTION
After reviewing the material, please complete the self-assessment test, which consists of a series of multiple-choice questions. To answer these questions online and receive real-time results, please visit http://www.dulaney-foundation.org and click “Online Courses.” Upon completing the activity and achieving a passing score of over 70% on the self-assessment test, you may print out a CME credit letter awarding 1 AMA PRA Category 1 Credit™. The estimated time to complete this activity is 1 hour.

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Dr. Regillo states that he receives grant research support from Alimera, Allergan, Genentech, Glaxo Smith Kline, Ophthotech, Regeneron, ThromboGenics, Advanced Cell Technology, Johnson and Johnson, QLT, and Alcon. He is a consultant for Alimera, Alcon, Genentech, GlaxoSmithKline, and Regeneron.

All of those involved in the planning, editing, and peer review of this educational activity report no financial relationships.
Pathophysiology of the Vitreomacular Interface

BY JAY S. DUKER, MD

“The vitreous is like the appendix, it serves an important purpose in utero. After that it causes nothing but trouble.”
— Jay S. Duker, MD

Almost all vitreomacular interface (VMI) disease and pathology is the result of aging. There are 2 main events that occur with the vitreous as we age. The first is liquefaction, when pockets of fluid develop within the vitreous cavity.

Even autopsy specimens from children as young as 4 years old show the beginning of the liquefaction of the vitreous, which proceeds slowly through life. Approximately 20% of the vitreous is liquefied by a person’s late teens, and by age 70, approximately 50% is liquefied. Despite this liquefaction, autopsy specimens on normal eyes show almost no posterior vitreous detachment in eyes younger than 60 years of age.

Along with this liquefaction process, there’s a progressive age-related weakening of the adhesion (the molecular glue consisting of collagen, fibronectin, and laminin) between the posterior vitreous cortex, which is also commonly referred to as the posterior hyaloid, and the internal limiting membrane. After the age of 60, this weakness really becomes more evident, and, as the liquefaction increases, this can result in a posterior vitreous separation.

Mark Johnson, MD, who performed seminal research on the progression of posterior vitreous detachment (PVD) said in his paper in the American Journal of Ophthalmology, “PVD is the most important event in the life of the human vitreous gel.”

Areas of Adhesion

There are 4 areas of the retina to which the vitreous is most tightly adherent: the vitreous base, along large retinal vessels, the optic disc margin, and the macula. It adheres to the macula in 2 locations: along a 500 µm diameter circle, which is known as a foveolar attachment, or along a 1500 µm diameter circle, which is known as a macular hole.
It is highly unusual, except in the case of trauma, for the vitreous to detach from the vitreous base. Acute PVD along the large retinal vessels can cause a vitreous hemorrhage even without a retinal tear. The vitreous is very adherent at the optic disc margin and at the macular areas. The evolution of a normal PVD is seen in Figure 1.

**Abnormal PVD**

Abnormal vitreous adhesion at the vitreous base in the setting of acute PVD can cause peripheral retinal tears and lead to retinal detachment.

Abnormal vitreous adhesion at the macula and optic disc can lead to VMI disease such as vitreomacular traction (VMT), full thickness macular hole (FTMH), lamellar macular hole (LMH), and epiretinal membrane (ERM). Optical coherence tomography (OCT) has helped tremendously in the understanding of these diseases of the VMI and has shown that focal, small (<500 μm) vitreous adhesions to the macula impart greater tractional stress to the foveola and can thus result more commonly in focal macular pathology such as macular hole (Figure 2). (Continued on page 8)
Vitreomacular Adhesions: When to Wait and When to Treat

BY PRAVIN U. DUGEL, MD

Prior to the US Food and Drug Administration approval of ocriplasmin (Jetrea, ThromboGenics), the only approach for patients with symptomatic vitreomacular adhesion (VMA) and vitreomacular traction (VMT) syndrome was either to watch and wait or perform vitrectomy to release the traction. Although these surgeries are particularly satisfying to perform because the outcomes are usually very good, every surgery carries risk. Because of this, the choice was often observation even if the patient had visual symptoms, as long as visual acuity was relatively good. This situation has proved frustrating to many of my patients because their problems are real. For example, a patient may be 20/30 but have distortion that makes visual function problematic. It is advisable not to operate in this case, but the needs of such a patient are not met by observation alone.

Watch and Wait

Surprisingly, there are only very few studies that have looked at the benefits and consequences of observation in the setting of symptomatic VMA. Of those studies, 3 in particular are the most consequential. In the first study, by Odrobina et al,1 which followed 19 patients with idiopathic VMT for approximately 8 months, 9 patients experienced vitreomacular release, but only 2 of these 9 patients had normal spectral-domain optical coherence tomography (SD-OCT) results at the final visit. Seventeen patients had 1 or more of the following retinal changes at the final visit: cystoid changes, lamellar macular hole, macular hole, inner segment/outer segment defect, or epiretinal membrane formation.

A recent study by John et al2 followed 38 patients over the course of approximately 19 months. Thirteen of the patients had no cystoid changes, 20 had cystoid changes, and 5 had subretinal fluid. At 19-month follow-up, 64% remained stable on SD-OCT and 13% had worsening of anatomic grading by SD-OCT. None of the eyes had spontaneous resolution of the VMT. Thirty-seven of the 38 eyes are still undergoing observation.

The study with the longest follow-up, by Hikichi et al,3 was performed before OCT was clinically available. Fifty-three patients in this study were divided at baseline according to whether they had cystoid changes (n = 10) or did not (n = 43) and were followed for 60 months. At follow-up, 80% of patients who did not have cystoid changes at baseline developed them. Of the patients who had cystoid changes at baseline, 79% had persistent cystoid changes at 60 months follow-up and 16% had resolution with degenerative sequelae: retinal pigment epithelial changes, degenerative changes, or cystoid changes.

The right time for intervention

Because we are just beginning to understand the role of the vitreomacular interface, there is little guidance about when to treat and when not to treat symptomatic VMA. In the studies mentioned previously, 11% to 47% of adhesions resolved spontaneously, which is a large range and does not provide much guidance. The time to spontaneous resolution was long, from approximately 8 to 15 months,1,3 and, as seen in Hikichi et al,3 patients’ vision may get worse over time with observation. In this study 15% of patients had visual acuity of 20/200 or worse at baseline and at the end of the study, 57% had vision of 20/200 or worse. Patients in the studies with shorter follow-up had better results.2 It is, therefore, hard to determine when best to intervene.

It is easier to determine whether to treat a patient with a macular hole. We know that full-thickness macular holes (FTMHs) close spontaneously in only 3% to 11% cases,4 and that approximately 75% of stage 2 macular holes will progress to stage 3 or 4.5 Further, Chew et al6 showed that the visual acuity of 45% of almost 200 patients in their study of FTMHs lost 2 or more lines of vision during follow-up.

Vitrectomy

What about vitrectomy? It stands to reason that, as surgeons, we like to operate. We have good results when we operate on VMT and macular holes. Moreover, surgery has become less invasive with smaller gauge instrumenta-
Vitreomacular Adhesion and Vitreomacular Traction With Macular Hole

By Pravin U. Dugel, MD

VITREOMACULAR ADHESION

In the clinical trial for ocriplasmin, we enrolled a 66-year-old woman who had decreased vision in her right eye that persisted for 6 months (Figures 1-4). She was diagnosed with high punctate vitreomacular adhesion (VMA). Per protocol, drug assignment was masked. This particular patient’s VMA resolved by day 28. It was learned that she was assigned to sham injection.

VITREOMACULAR TRACTION WITH MACULAR HOLE

One of the first patients in whom I injected ocriplasmin after US Food and Drug Administration approval was a 70-year-old woman who had been referred for evaluation to rule out macular hole. The patient had complaints of gradually decreasing vision in her left eye for the past 2.5 years, and it had recently worsened. After obtaining a spectral-domain optical coherence tomography (SD-OCT) scan, we diagnosed vitreomacular traction and small macular hole (Figure 5).

The patient lives north of the Phoenix area and, because of the altitude, did not want to undergo surgery because of the air bubble precautions.

Postinjection, she had floaters and a kaleidoscope effect with her vision that lasted 3 days after the injection. She has reported improved visual acuity since the injection. Her SD-OCT scan 14 days after the injection showed closure of the macular hole (Figure 6).
tion. Several studies have shown that surgery for VMT and macular hole is generally very effective and safe.7-11

However, surgery is not without risk. Risks with any vitrectomy procedure include retinal tears, detachments, endophthalmitis, and cataract formation in phakic patients. Additionally, patients who undergo surgery lose time from work and are inconvenienced by facedown positioning and restrictions on air travel because of a gas bubble.

DECISION-MAKING IN MACULAR HOLE AND VMA/VMT

Now that we have ocriplasmin available, we have to decide whether to intervene surgically or pharmaceutically. The key to success with ocriplasmin lies in proper patient selection. Although ocriplasmin may have a wide application as a combination agent in chronic retinal diseases such as diabetic macular edema, retinal vein occlusion, and age-related macular degeneration, it is important to confine the use of this drug to only the 2 patient groups shown in the MIVI TRUST trials to have the greatest success: patients with VMA and a macular hole of 400 µm or less and patients with VMA and vitreomacular adhesion of 1500 µm or less. If such patients are properly selected, the success rate with a single injection of ocriplasmin should be approximately 50%.

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VMA has been implicated as an initiating anatomic configuration in a number of different disease states including VMT, FTMH, LMH, and ERM.

SUMMARY

VMA has been implicated as an initiating anatomic configuration in a number of disease states including VMT, FTMH, LMH, and ERM. A better understanding of the identifying factors that might predict which eyes with VMA are prone to developing a disease of the VMI as opposed to merely progressing through the nonpathologic sequence of PVD will hopefully allow improved treatment of these conditions and better results for our patients.

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Figure 7. Vitreomacular adhesion.
Ocriplasmin (Jetrea, ThromboGenics) is a truncated form of human plasmin, made with recombinant DNA technology that targets fibronectin, laminin and collagen, among other molecules. Ocriplasmin enhances vitreous liquefaction and promotes clean separation of the vitreous cortex from the internal limiting membrane.²

There are 12 studies of ocriplasmin, 11 of which have been completed (Figure 1), including MIVI-006 and MIVI-007, which comprise the phase 3 clinical trial program.² More than 1000 patients have received injections with various doses of ocriplasmin in the clinical trials.

**MIVI-TRUST PROGRAM**

MIVI-006 was conducted in the United States, and MIVI-007 was conducted in the United States and Europe. These were nearly identical, randomized, prospective, placebo-controlled studies that evaluated a single dose of 125 µg of ocriplasmin compared with an active placebo injection control to treat patients with symptomatic vitreomacular adhesion (VMA), including macular hole cases. The primary anatomic endpoint was VMA resolution at day 28, which was determined by OCT at a formal single reading center at Duke. The secondary endpoints were total posterior vitreous detachment at day 28, nonsurgical closure of full-thickness macular holes, visual acuity improvement of 2 lines or greater, need for secondary vitrectomy, and visual function questionnaire assessment. Patients were followed in the study for 6 months.

Inclusion criteria included a diagnosis of symptomatic focal VMA, best corrected visual acuity (BCVA) of 20/25 or less in the study eye, and BCVA of 20/800 or greater in the fellow eye. Patients with epiretinal membrane (ERM) were also included. It is important to note that patients with very good baseline visual acuity were allowed into the studies, and this factor could have resulted in a “ceiling effect” with regard to visual acuity gains.

Exclusion criteria included high myopia, history of prior vitrectomy or prior laser photocoagulation to the macula, macular hole diameter of greater than 400 µm, and other retinal diseases that could affect visual function.

Patients in these trials fell into 3 categories: patients...
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with vitreomacular traction (VMT) with no baseline macular hole and no baseline ERM, patients with macular hole with or without ERM, and patients with ERM at baseline (ERM was not being treated; rather, VMA associated with ERM). All patients had VMA confirmed by optical coherence tomography (OCT).

RESULTS: EFFICACY

With regard to the primary endpoint in the pooled data from both phase 3 trials, 26.5% patients in the ocriplasmin group had VMA resolution at day 28 compared with 10.1% of patients in the placebo group.

VMT. In the pure VMT subgroup (no ERM or macular hole), there was a success rate of approximately 30% in the ocriplasmin arm compared with 7.7% in the placebo arm, a statistically significant difference. Eyes with more focal VMT (<1500 µm) had a greater success rate with ocriplasmin (~34%) compared with eyes with a broader-based VMT (>1500 µm; ~10%; Figure 2).

In ocriplasmin-treated VMT patients who achieved VMA resolution, approximately 41% gained 2 or more lines of BCVA at 6 months (Figure 3). The mean visual acuity gain was 7.3 letters in ocriplasmin-treated VMT patients who achieved VMA resolution (Figure 4). This is significant considering the good baseline visual acuity of these patients.

Macular hole. Ocriplasmin had the best success rates in patients with macular hole. Approximately 40% of patients had successful macular hole closure at day 28 that persisted through 6 months (Figure 5). These results indicate that ocriplasmin works quickly for macular holes and that its effects are sustained over time.

Further subgroup analysis showed that macular holes smaller than 250 µm had a closure rate of 60% as compared with holes larger than 250 µm, which had a closure rate of approximately 25% (Figure 6). There were, however, 19 patients who had holes larger than 400 µm—a protocol violation. If these 19 patients were excluded, the closure rate of the holes larger than 250 µm jumps to about 34%.

Seventy-seven percent of patients gained 2 or more lines after achieving macular hole closure with a single injection of ocriplasmin (Figure 7), which is to be
CASE REPORT

Vitreomacular Traction
By Carl D. Regillo, MD

A 62-year-old woman presented with mild, fluctuating symptoms of blurred vision in her right eye, which was identified as vitreomacular traction (VMT). She had no symptoms in the left eye. The left eye was also normal on spectral-domain optical coherence tomography (SD-OCT; Figure 1). It was decided that this patient would be observed for more changes.

Her symptoms gradually worsened in the right eye over the course of the next 8 months, and she had new, mild symptoms in her left eye (Figure 2). For her right eye, she was given the choice of either having us continue to observe, undergoing vitrectomy, or receiving an injection of ocriplasmin under the protocol the Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion/VMT Including Macular Hole (OASIS) phase 3b clinical trial. We would continue to observe the left eye.

After receiving an injection of ocriplasmin in her right eye, she reported symptoms of floaters and flashes, dyschromatopsia, and decreased vision the night of the injection. On day 1 after the injection, an OCT taken by her husband, an optometrist, demonstrated resolution of the VMT (Figure 3). She had counting fingers vision on day 1, and the floaters and flashes and dyschromatopsia persisted. Visual acuity and the visual disturbances, however, steadily improved throughout the first week, as did anatomy on OCT (Figure 4). At 1-month follow-up, the patient’s OCT and visual acuity continued to improve (Figure 5). At 3 months’ follow-up, we saw further improvement on OCT and visual acuity (Figure 6), and sometime between 1 and 3 months the left eye had improved to 20/25 (Figure 7).

expected based on the patients’ average baseline visual acuity (54.8 letters, 20/80). The mean visual acuity gain for patients who had closure of macular holes with a single injection of ocriplasmin was 14.1 letters (Figure 8). One patient in the macular hole subgroup lost 1 letter of vision. The macular hole (387 µm) closed by day 7 and the patient also had pterygium, cortical cataract, cupping of optic disc, retinal pigment epithelial changes, vascular narrowing, and macular edema in the study eye at diagnosis.

ERM. In the clinical trials, ocriplasmin did not work well for patients with ERM. In patients who had some degree of ERM evident on OCT, the success rate overall was only about 8% to 9% compared with 1.5% in the placebo group.

RESULTS: SAFETY

Figure 9 shows the proportion of adverse events up to day 7 after injection with ocriplasmin vs placebo. There was a higher rate of adverse events in the ocriplasmin-treated eyes in all categories, but this is
what is expected from a drug that is designed to cause vitreous liquefaction and separation. The vast majority of adverse events were rated at mild or moderate, and many were transient.

Between day 8 and month 6, the rates of adverse events were nearly identical between the ocriplasmin and placebo groups, and, for some events, higher in the placebo group (Figure 10).

Six patients in total had transient vision loss after ocriplasmin injection. The overall rate of this adverse event was less than 1% (6 of more than 800 patients who have been treated with ocriplasmin to date). All but 1 of these patients regained their vision, with a few winding up with better visual acuity than at baseline. Furthermore, there were no abnormal findings on imaging studies or otherwise that could be pinpointed as a cause for vision loss. The only factor that all of these patients had in common was an extremely rapid resolution of VMA within 24 hours.

The incidence of retinal tear or detachment was low in both arms. The rate of retinal tears and detachments were higher in the placebo arm than in the ocriplasmin arm, which was most likely due to the higher rate of vitrectomy in this arm (Figure 11).

Summary
A single injection of ocriplasmin resulted in significantly increased rates of VMA and full thickness macular hole resolution in comparison with to placebo. The anatomic success rate appears to be greater for eyes that have more focal VMA adhesion and smaller macular holes. The resolution of VMA and full thickness macular holes resulted in significant visual acuity improvement over 6 months. Finally, most adverse events were transient and mild and occurred within the first week after injection.

![Figure 7](image7.png)  Seventy-seven percent of patients gained 2 or more lines after achieving macular hole closure with a single injection of ocriplasmin, which is to be expected based on the patients’ average baseline visual acuity (54.8 letters, 20/80).

![Figure 8](image8.png)  The mean visual acuity gain for patients who had closure of macular holes with a single injection of ocriplasmin was 14.1 letters.

![Figure 9](image9.png)  The proportion of adverse events up to day 7 after injection with ocriplasmin vs placebo.

![Figure 10](image10.png)  Between day 8 and month 6, the rates of adverse events nearly identical between the ocriplasmin and placebo groups, and for some events, higher in the placebo group.
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Q&A

**Dr. Duker:** Dr. Regillo, you have a lot of experience injecting ocriplasmin in the clinical trials and are well versed in the data. For whom do you think this drug is best suited?

**Dr. Regillo:** The data suggest that ocriplasmin works best in patients with focal, symptomatic, and progressive vitreomacular adhesion (VMA) and for patients with acute, small, full-thickness macular holes.

**Dr. Duker:** If you had a patient who presents with highly symptomatic vitreomacular traction (VMT) and 20/30 vision on the first visit, would you treat him or her, or would you wait?

**Dr. Regillo:** Perhaps.

**Dr. Duker:** How can I get you to go from, “perhaps” to, “Yes, I would definitely treat this patient?” What is your cut-off point from watch and wait?

**Dr. Regillo:** Let’s say the patient is 20/60 and symptomatic and he or she says that the visual distortion began 3 months ago and is progressively getting worse. I would treat this patient with ocriplasmin.

**Dr. Duker:** What if a patient has been referred for an abnormal optical coherence tomography (OCT) scan that shows VMT, the patient has 20/25 vision and some distortion?

**Dr. Regillo:** I would be less inclined to treat this patient. Dr. Dugel’s article addressed the broad spectrum of spontaneous resolution—11% to 40% in VMT—and I think that much of this variation is related to severity. When the VMT is mild, I think that there is a greater likelihood of spontaneous separation of the vitreous. The studies with the longest follow-up for ocriplasmin, however, did not use OCT. Even so, I would make a prediction that the more severe the VMT, the less likely there will be spontaneous separation of the vitreous.

**Dr. Duker:** Do you think you or anyone can pick a priori patients who have VMA that will not progress to spontaneous and clean separation?

**Dr. Regillo:** No. When a patient presents with early and mild VMA, it is not possible to predict its course.

**Dr. Duker:** What is your threshold for injecting a patient with a macular hole?

**Dr. Regillo:** Based on the data from the clinical trials, I will use ocriplasmin for full thickness macular holes that are 400 µm or less in size.

**Dr. Duker:** Will you watch these smaller holes initially?

**Dr. Regillo:** No. I will treat. The likelihood that macular holes will close spontaneously is low and the larger the hole is (up to 400 µm), the less likely spontaneous closure will occur.

**Dr. Duker:** For a retina specialist who is used to performing intravitreal injections, is there anything unique about this drug that he or she should know about, or is this like any other injection that we do?

**Dr. Regillo:** Ocriplasmin is not a stable drug. It is shipped and stored frozen. When it is ready to be administered, it should be taken out of the freezer, defrosted, diluted, and then injected promptly. (See package insert for details.)

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Supplement to Retina Today March 2013

CURRENT TREATMENT OPTIONS FOR VITREOMACULAR ADHESION AND MACULAR HOLE

INSTRUCTIONS FOR CME CREDIT

1 AMA PRA Category 1 Credit™

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CME Questions

1. In the MIVI-Trust trials, macular holes of what size had a better rate of closure?
   a. 400 µm or smaller
   b. 250 µm or smaller
   c. 150 µm or larger
   d. none of the above

2. Vitreomacular adhesions (VMAs) are implicated in what disease states?
   a. Macular hole
   b. Vitreomacular traction
   c. Epiretinal membrane
   d. Retinal tears
   e. Retinal detachment
   f. All of the above

3. The greatest benefit for patients treated with ocriplasmin is seen for vitreomacular traction (VMT) of what size:
   a. smaller than or equal to 2500 µm
   b. larger than 1500 µm
   c. smaller than or equal to 1500 µm
   d. smaller than or equal to 250 µm

4. In ocriplasmin-treated VMT patients who achieved VMA resolution, approximately 41% gained __ or more lines at 6 months.
   a. 3
   b. 0
   c. 2
   d. 4
   e. none of the above

5. Which of the following is not considered one of the 4 most tightly adherent areas of vitreous attachment to the retina?
   a. Along the macula in a 500 µm diameter circle
   b. Along the macula in a 1500 µm diameter circle
   c. The vitreous base
   d. Along small retinal vessels
   e. The optic disc margin

6. Which of the following is not a common result of focal, small (<500 µm) vitreous adhesions to the macula?
   a. macular hole
   b. lamellar macular hole
   c. myopic macular schisis
   d. vitreomacular traction

Did the program meet the following educational objectives?

Explain the process by which VMA occurs ______ Neutral ______ Disagree ______

Identify the disease states with which VMA is associated ______ Neutral ______ Disagree ______

Identify the clinical implications of anomalous PVD ______ Neutral ______ Disagree ______

Identify the risks of performing vitrectomy to induce PVD ______ Neutral ______ Disagree ______

Explain the mechanism of action of pharmacologic vitreolysis ______ Neutral ______ Disagree ______

Differentiate between the various agents that can be used for pharmacologic vitreolysis in terms of their composition, advantages, and disadvantages ______ Neutral ______ Disagree ______

Discuss the available data on the safety and efficacy of vitreolysis agents for PVD induction ______ Neutral ______ Disagree ______
**ACTIVITY EVALUATION**

Your responses to the questions below will help us evaluate this CME activity. They will provide us with evidence that improvements were made in patient care as a result of this activity as required by the Accreditation Council for Continuing Medical Education (ACCME). Please complete the following course evaluation and return it via fax to 610-771-4443.

Name and email  ____________________________________________________________________________________________

Do you feel the program was educationally sound and commercially balanced?  □ Yes  □ No

Comments regarding commercial bias:
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Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low ______

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Would you recommend this program to a colleague?  □ Yes  □ No

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If yes, please specify. We will contact you by email in 1 to 2 months to see if you have made this change.
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Please list any additional topics you would like to have covered in future Dulaney Foundation CME activities or other suggestions or comments.
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