Visudyne®
verteporfin for injection

Management of Progressive Choroidal Neovascularization in Exudative Age-Related Macular Degeneration

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Age-related macular degeneration (AMD) is a degenerative disease that can result in vision impairment and legal blindness. The "dry" or non-neovascular form of AMD is characterized by drusen and retinal pigment epithelium (RPE) abnormalities including pigmentation and atrophy. "Wet" or choroidal neovascularization exudative AMD is manifested by choroidal neovascularization (CNV). CNV is characterized by subtypes according to the origin and location of neovascular vessels. *Type 1 CNV* refers to vessels beneath the RPE. *Type 2 CNV* (classic) refers to vessels expanding into the subretinal space between the neurosensory retina and the RPE.[1-3]

Vascular endothelial growth factor (VEGF) is a key component in promoting neovascularization, thus the use of intravitreal anti-VEGF agents is a common way to treat CNV.[4] However, it is known that complete regression of CNV is difficult to achieve using anti-VEGF therapy in most cases.[3]

The following case report describes a patient with recurrent CNV that was diagnosed first as type 1 and then developed to type 2 CNV despite the patient's receiving ranibizumab injections in a treat-and-extend regimen for 5 years in the left eye (***Figures 1-5***). After undergoing photodynamic therapy (PDT) with VISUDYNE® (verteporfin for injection), the patient's visual acuity was stabilized with resolution of CNV and exudation (***Figure 6***). Since the PDT with VISUDYNE® the patient has not required intervening injections (5 months, as of the review of this case for publication).

Case Report: Photodynamic Therapy with VISUDYNE® in a Patient With Progressive Choroidal Neovascularization in Exudative Age-Related Macular Degeneration

BACKGROUND: An 82-year-old male with subfoveal type 1 CNV was treated for 5 years with anti-VEGF therapy on a treat-and-extend regimen. The patient experienced progressive vision loss throughout the course of treatment and progression to type 2 CNV.

DIAGNOSIS: The diagnosis of type 1 CNV in AMD was based on intravenous fluorescein angiography (IVFA) on August 6, 2015. The progression to type 2 CNV occurred during treatment with anti-VEGF and was reconfirmed on October 22, 2020. (***Figures 1-5***).

Indication

VISUDYNE® (verteporfin for injection) therapy is a photoenhancer indicated for the treatment of patients with predominantly classic subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration, pathologic myopia or presumed ocular histoplasmosis. There is insufficient evidence to indicate VISUDYNE for the treatment of predominantly occult subfoveal CNV.

Important Safety Information

- VISUDYNE® (verteporfin for injection) is contraindicated for patients with porphyria or known hypersensitivity to any component of this preparation.

Please see additional Important Safety Information throughout and full Prescribing Information here.

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TREATMENT:

After the initial diagnosis of type 1 CNV in AMD, the patient began treatment with ranibizumab injections beginning on August 16, 2015. A treat-and-extend regimen was used to reduce the burden of frequent treatments.

However, during this period recurrence continued and vision loss progressed from 20/50-2 in October 2015 to 20/250-3 by October 2018, as seen in ***Table 1***.

The patient's vision loss was secondary to the persistent CNV and progressive subfoveal RPE atrophy. It became evident that the patient's condition was not improving as macular vision was lost.

It was time to consider other treatment options. I discussed my experience treating patients with advanced classic CNV using PDT with VISUDYNE® monotherapy. VISUDYNE® is indicated for the treatment of patients with predominantly classic subfoveal choroidal neovascularization due to AMD, pathologic myopia, or presumed ocular histoplasmosis.[5]

The patient felt comfortable about this course of therapy, which works as a two-step process: an intravenous infusion of verteporfin followed by light activation with a nonthermal diode laser. The patient understood that sometimes multiple courses of therapy are needed and can be repeated at 3-month intervals, if necessary.[5]

I also informed the patient that because skin and eyes can become temporarily sensitive to light that sunglasses and protective clothing should be worn on the day of treatment and that exposure to sunlight should be avoided for 5 days after treatment.[5]

The patient agreed to PDT with VISUDYNE® and returned on October 22, 2020, for treatment. At this time, his BCVA was 20/400. An IVFA image shows a classic neovascular pattern of a type 2 CNV (***Figure 1***). A second IVFA image shows diffuse type 1 CNV with longstanding subfoveal RPE atrophy with new type 2 CNV, inferior temporal (***Figure 2***). The subfoveal RPE atrophy with adjacent type 2 CNV is also visible on optical coherence tomography (OCT) (***Figure 3***) and new extensions of type 2 CNV, inferior temporal, on optical coherence tomography angiography (OCTA) (***Figure 4***).

After the images were taken and reviewed, the patient underwent PDT with VISUDYNE®. Afterward, he did not report any treatment-related adverse effects and appeared to tolerate the treatment well.

Important Safety Information (cont.)

- Standard precautions should be taken during infusion of VISUDYNE to avoid extravasation, including but not limited to:
  - A free-flowing intravenous (IV) line should be established before starting VISUDYNE infusion and the line should be carefully monitored.
  - Due to the possibly fragility of vein walls of some elderly patients, it is strongly recommended that the largest arm vein possible, preferably the antecubital, be used for injection.
  - Small veins in the back of the hand should be avoided.

Please see additional Important Safety Information throughout and full Prescribing Information here.

Date	BCVA
October 2015	20/50-2
October 2016	20/60+2
January 2017	20/80+2
April 2017	20/100-2
October 2018	20/250-3

Table 1.
BCVA=best corrected visual acuity.

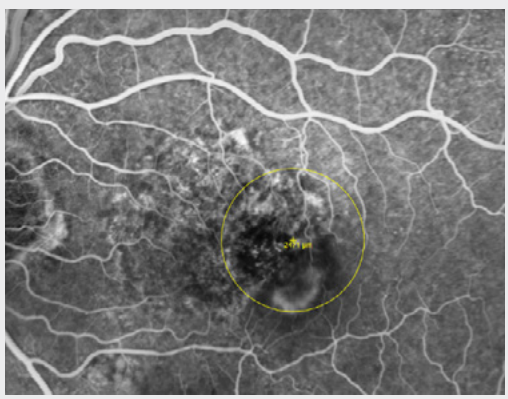

Figure 1. IVFA early. Image shows classic neovascular pattern of a type 2 CNV. Image taken October 22, 2020, date of PDT treatment.

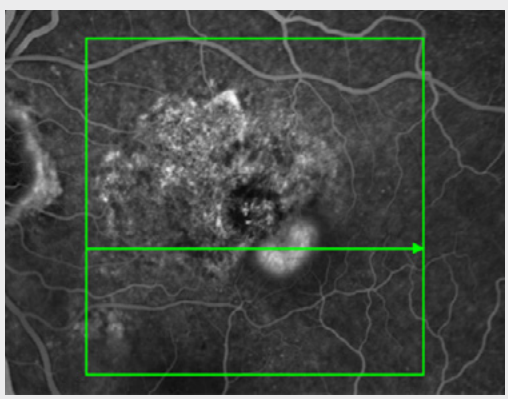

Figure 2. IVFA late. Image shows diffuse type 1 CNV with longstanding subfoveal retinal pigment epithelium (RPE) atrophy with new type 2 CNV, inferior temporal. Image taken October 22, 2020.

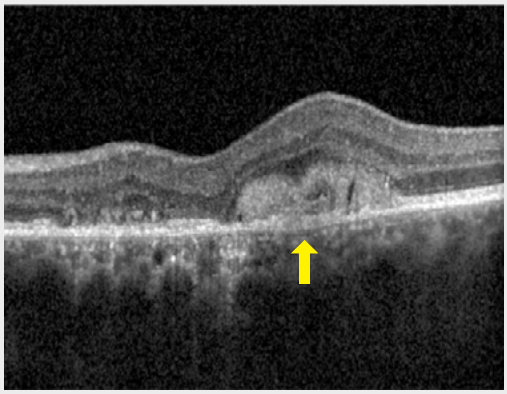

Figure 3. OCT late. Image shows neovascularization anterior to RPE (yellow arrow). Image taken October 22, 2020.

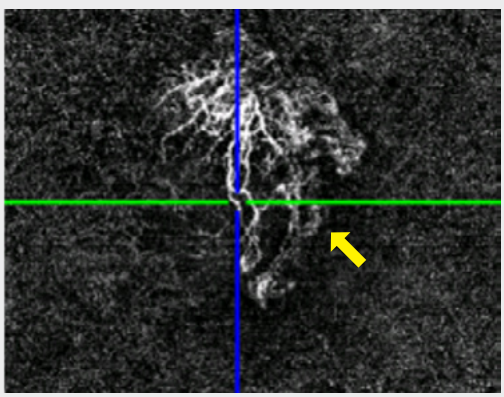

Figure 4. OCTA. Image shows type 1 CNV with new extension of type 2 CNV, inferior temporal (yellow arrow). Image taken October 22, 2020.

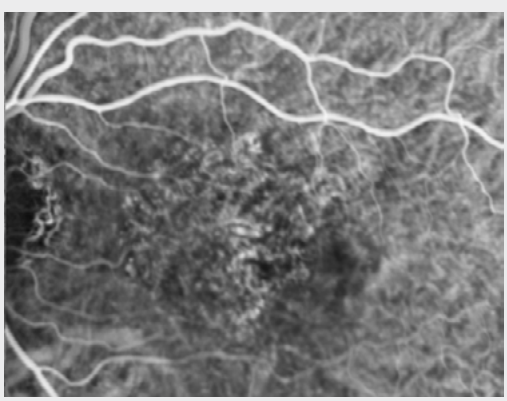

Figure 5. Indocyanine green angiography (ICG). Image shows nonspecific backbone of subfoveal CNV. Image taken October 22, 2020.

WHY VISUDYNE®?

The decision to replace anti-VEGF injections with PDT with VISUDYNE® was based on the loss of vision and recurrence of CNV.

Interestingly, the TREND study, which randomized patients with neovascular AMD to receive anti-VEGF therapy on either a treat-and-extend basis or a monthly one, found that intraretinal cysts persisted at the end of the 12-month trial at about 49%, irrespective of treatment protocol, and subretinal fluid persisted at about 39%, also irrespective of treatment protocol.[6]*

The goal in this case was to achieve stability of BCVA and to resolve CNV, exudation, and hemorrhage. PDT with VISUDYNE® has been shown to be effective in patients with this condition.[5,7]

*__Study Design:__ In a 12-month, multicenter, randomized clinical trial, 650 patients with neovascular AMD were randomized 1:1 to receive ranibizumab 0.5 mg T&E (treat and extend) or monthly. Primary outcome was to show noninferiority of ranibizumab 0.5 mg T&E versus monthly regimen, as assessed by the change in BCVA from baseline to the end of the study. Secondary objectives included change in retinal central subfield thickness from baseline to the end study, treatment exposure, and safety.

Important Safety Information (cont.)

- Extravasation of VISUDYNE, especially if the affected area is exposed to light, can cause severe pain, inflammation, swelling or discoloration at the injection site. Necrosis at the injection site following extravasation has been reported. If extravasation does occur, the infusion should be stopped immediately. The extravasation area must be thoroughly protected from direct light until swelling and discoloration have faded in order to prevent the occurrence of local burn, which could be severe. Cold compresses should be applied to the injection site. Oral medication for pain relief may be administered.
- Following injection with VISUDYNE, care should be taken to avoid exposure of skin or eyes to direct sunlight or bright indoor light for 5 days. If emergency surgery is necessary within 48 hours after treatment, as much of the internal tissue as possible should be protected from intense light.
- Patients who experience severe decrease of vision of 4 lines or more within 1 week after treatment should not be retreated, at least until their vision completely recovers to pretreatment levels and potential benefits and risks of subsequent treatment are carefully considered by the treating physician.
- Cases of anaphylactic reactions have been reported. Immediately discontinue VISUDYNE and initiate appropriate therapy if anaphylactic or other serious allergic reactions occur during or following therapy.

Please see additional Important Safety Information throughout and full Prescribing Information here.

FOLLOW-UP:

The patient returned for his first post-PDT follow-up on December 22, 2020. The patient's BCVA was 20/400. On OCT the image showed resolved type 2 CNV. No anti-VEGF or PDT treatment was given. At the second follow-up in May 2021, OCT scans indicated no neovascularization and exudation (***Figure 6***), and the patient's BCVA was 20/400.

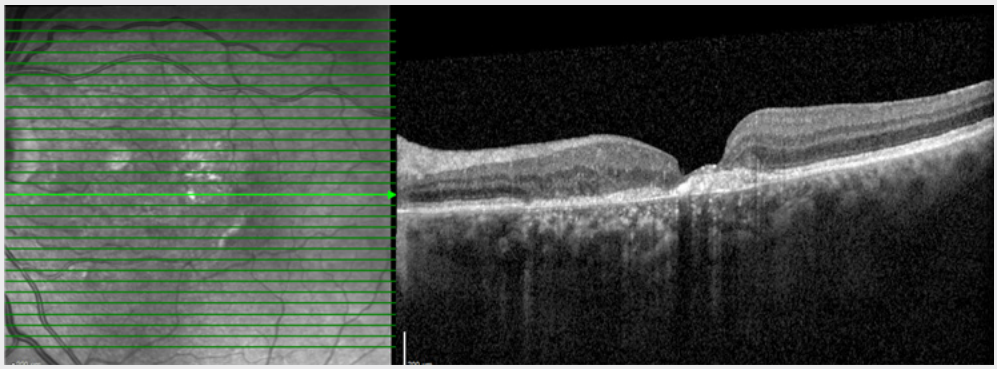

Figure 6. OCT image, post-treatment with PDT. OCT enface and cross-sectional images show the absence of neovascularization (green arrow). Image taken May 21, 2021.

CONCLUSIONS

This case involved a patient diagnosed with subfoveal type 1 CNV in August 2015 who was treated with anti-VEGF treatments in his left eye for a 5-year period. Despite this treatment regimen, CNV progressed to type 2 and macular vision was lost. Because of this decline the patient was treated with PDT with VISUDYNE® in his left eye. After PDT treatment, his vision was stabilized and required no treatment for 7 months. Patient will be retreated with PDT with VISUDYNE® when neovascular vessels reopen and recurrence of exudation. Until then, no treatment is necessary. This case is an example of a viable alternative treatment in the face of persistent type 2 CNV and progressive subfoveal RPE atrophy that can offer a patient benefits – and it's a treatment that is well tolerated.[5,7]

Important Safety Information (cont.)

- The most frequently reported adverse events (occurring in approximately 10%-30% of patients) were injection site reactions (including pain, edema, inflammation, extravasation, rashes, hemorrhage, and discoloration), and visual disturbances (including blurred vision, flashes of light, decreased visual acuity, and visual field defects, including scotoma).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see additional Important Safety Information throughout and full Prescribing Information here.

References: 1. Yang S, Zhao J, Sun X. Resistance to anti-VEGF therapy in neovascular age-related macular degeneration: a comprehensive review. *Drug Des Devel Ther.* 2016;10:1857-1867. **2.** Soubrane G, Bressler NM. Treatment of subfoveal choroidal neovascularisation in age related macular degeneration: focus on clinical application of verteporfin photodynamic therapy. *Br J Ophthalmol.* 2001;85(4):483-495. **3.** Nakano Y, Kataoka K, Takeuchi J, et al. Vascular maturity of type 1 and type 2 choroidal neovascularization evaluated by optical coherence tomography angiography. *PLoS One.* 2019;14(4):e0216304. **4.** Homayouni M. Vascular endothelial growth factors and their inhibitors in ocular neovascular disorders. *J Ophthalmic Vis Res.* 2009;4(2):105-114. **5.** VISUDYNE Prescribing Information. Bausch & Lomb Incorporated. **6.** Silva R, Berta A, Larsen M, Macfadden W, Feller C, Monés J; TREND Study Group. Treat-and-extend versus monthly regimen in neovascular age-related macular degeneration: results with ranibizumab from the TREND study. *Ophthalmology.* 2018;125(1):57-65. **7.** Bressler NM. Treatment of Age-Related Macular Degeneration With Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two year results of 2 randomized clinical trials–TAP report 2. *Arch Ophthalmol.* 2001;119(2):198-207.

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