Treatment of Persistent Retinal Fluid Despite Anti-VEGF Therapy in a Patient With Neovascular Age-Related Macular Degeneration

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Age-related macular degeneration (AMD) is one of the most common causes of blindness globally.[1] AMD can be classified into 2 types: non-neovascular (dry) or neovascular (wet).[1]

Neovascular AMD is characterized by presence of signs of exudation such as subretinal fluid and subretinal hemorrhage, and complications such as pigment epithelial detachment.[1] Neovascular AMD exhibits the presence of choroidal neovascularization that breaches through Bruch's membrane into the subretinal pigment epithelium space and/or the subretinal space.[1]

Before anti-vascular endothelial growth factor (anti-VEGF) therapy became the standard of care for neovascular AMD, photodynamic therapy (PDT) was the only treatment option available.[1] Anti-VEGF therapy has shown significant benefit in neovascular AMD, including disease control and improvement in vision.[1] However, there remains a subset of patients with persistent disease activity in spite of anti-VEGF therapy.[1] The need for monthly office visits, treatment burden, and ocular and systemic safety remain concerns with anti-VEGF therapy.[1]

PDT can be offered to patients who continue to have persistent disease activity, even with anti-VEGF therapy, with the potential to help reduce their treatment burden.[2] The following case report describes a patient with neovascular AMD who received continuous anti-VEGF therapy for 4 years in her right eye. Despite treatment, there was persistent retinal fluid. After undergoing PDT with VISUDYNE® (verteporfin for injection), the patient required no additional anti-VEGF injections, showed improved visual acuity, and remained fluid-free as of the last follow-up (2 years post-PDT, as of the review of this case for publication).

Case Report: Photodynamic Therapy With VISUDYNE® in a Patient With Persistent Retinal Fluid in Neovascular Age-related Macular Degeneration Despite Anti-VEGF Therapy

BACKGROUND: A 76-year-old female was diagnosed with unilateral neovascular AMD in 2018 by another physician and received anti-VEGF therapy every 8 weeks for 4 years. Her treatment interval was unable to be extended beyond 8 weeks.

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.

DIAGNOSIS: In January 2021, I took over management of the patient and agreed with the previous diagnosis of neovascular AMD. Her best-corrected visual acuity was 20/40 in her right eye and 20/25 in her left eye. Both eyes showed grade-2 nuclear sclerosis, and the remainder of the examination findings were within normal ranges. An optical coherence tomography (OCT) scan of the right eye showed subretinal fluid involving the subfoveal area (***Figure 1***).

On an OCT raster scan, a small area of shallow pigment epithelial detachment (PED) with minimal intraretinal fluid was observed (***Figure 2***).

Given the patient's long-standing disease and need for continuous injections, fluorescein angiography and indocyanine angiography were recommended. Angiography can reveal important information about the vascular network or suggest alternative diagnoses, which can help to inform other forms of treatment.[1] These tests may provide beneficial information in cases of poor response or multiple recurrences.[1] Angiography in this patient confirmed the presence of a vascular network supranasal to the fovea (***Figure 3***).

TREATMENT: After reviewing the angiography findings, introducing PDT to her treatment regimen was considered. PDT with VISUDYNE® is indicated for the treatment of patients with predominantly classic subfoveal choroidal neovascularization due to AMD, pathologic myopia, or presumed ocular histoplasmosis.[3] I counseled the patient that PDT is a 2-step process performed in the office that requires administration of verteporfin via intravenous infusion followed by activation of the drug with light from a nonthermal diode laser.[3] She was advised that her skin would be sensitive to bright light and direct sunlight for 5 days after therapy.[3] The patient agreed and underwent PDT with VISUDYNE® in April 2021.

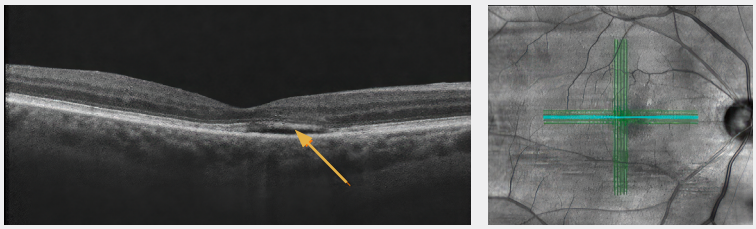

Figure 1. OCT image of the patient's right eye in January 2021. Orange arrow indicates subretinal fluid in the subfoveal region.

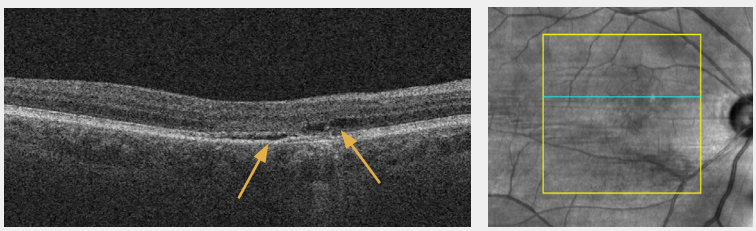

Figure 2. OCT raster scan image (superonasal to the fovea) image of the patient's right eye in January 2021. Orange arrows indicate an area of PED with associated intraretinal fluid.

Figure 3. Angiographic still images demonstrating vascular leakage and the presence of a vascular network supranasal to the fovea.

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.

WHY VISUDYNE®?

Anti-VEGF therapy is the standard of care for neovascular AMD.[1] However, PDT can play an important role in controlling disease activity,[1] particularly for predominately classic choroidal neovascularization.[3] Considering this patient's long duration of treatment and her continuous need for anti-VEGF therapy, the introduction of VISUDYNE® had the potential to reduce her need for anti-VEGF injections and extend her treatment-free interval.

FOLLOW-UP:

The patient was followed up with monthly. There were no signs of disease activity on OCT, and anti-VEGF therapy was not administered. Her visual acuity improved to 20/30 in the treated right eye, and there was no retinal fluid on OCT (***Figure 4***).

The extrafoveal area of shallow PED with intraretinal fluid (as shown in Figure 2) showed regression of fluid and flattening of the PED (***Figure 5***).

She was under regular monitoring, and we increased her follow-up interval to every 3 months.

There has been no disease activity after 2 years of follow-up post-PDT, and, thus, no anti-VEGF therapy has been administered since PDT.

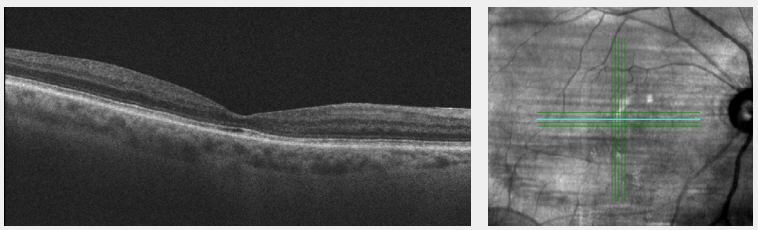

Figure 4. OCT image of the patient's right eye following PDT with VISUDYNE®. No retinal fluid is evident.

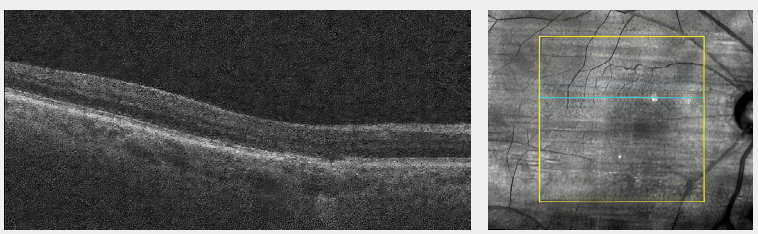

Figure 5. OCT raster scan image (superonasal to the fovea) image of the patient's right eye following PDT with VISUDYNE®. Note flattening of PED and regression of associated retinal fluid.

CONCLUSIONS

This case described a patient with neovascular AMD who received continuous anti-VEGF therapy for 4 years. Given her previous need for continuous anti-VEGF therapy, we performed PDT with VISUDYNE®. After a single PDT treatment, she remained fluid-free and showed improvement in visual acuity without the need for anti-VEGF therapy. This case study demonstrates an example of a successful outcome of PDT in neovascular AMD.

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.

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

Important Safety Information (cont.)

- 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.
- 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. Fleckenstein M, Keenan TDL, Guymer RH, et al. Age-related macular degeneration. *Nat Rev Dis Primers*. 2021;7(1):31. **2.** Gao Y, Yu T, Zhang Y, Dang G. Anti-VEGF monotherapy versus photodynamic therapy and anti-VEGF combination treatment for neovascular age-related macular degeneration: a meta-analysis. *Invest Ophthalmol Vis Sci*. 2018;59(10):4307-4317. **3.** VISUDYNE [package insert]. Bridgewater, NJ: Bausch & Lomb Incorporated.

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