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Clinical Update: FDA Approval of Susvimo™ for Neovascular Age-Related Macular Degeneration

Background

Age-related macular degeneration (AMD) is a leading cause of vision loss in older adults. Macular findings such as drusen and abnormal changes in the retinal pigment epithelium are common among patients with macular degeneration and approximately 10% of AMD patients go on to develop the neovascular or exudative ("wet") form of the disease (nAMD) (Figure 1).[1] In the absence of treatment, most AMD patients with severe vision loss have the exudative form of the disease.[2] Fortunately, retina specialists now have multiple reliable treatments for nAMD in the form of intravitreal medications targeting vascular endothelial growth factor (VEGF), a key mediator in the development of abnormal blood vessels.[3,4,5] While these medications have tremendously improved visual outcomes for patients with nAMD, they do present a burden to both patients and physicians as frequent follow-up visits and treatments as often as monthly are often necessary. Thus, while much progress has been made over the last several years, there is still significant room for improvement in care for nAMD patients, particularly with regards to identifying more durable treatment options.

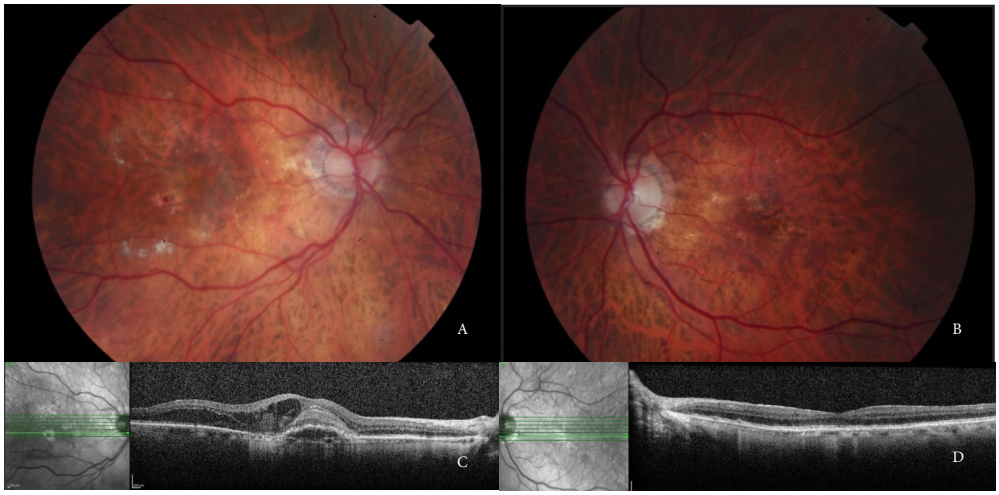

Figure 1: Color and optical coherence tomography photos of a patient with nAMD and a chronic choroidal neovascular membrane in her right eye (A, C) and non-exudative AMD with characteristic drusen and RPE changes in her left eye (B, D).

Archway Trial and Approval of Susvimo™

One of the newest exciting additions to the retina specialist's armamentarium against nAMD is a Port Delivery System (PDS) with ranibizumab. Now under the brand name Susvimo™, this PDS received approval by the Food and Drug Administration in late 2021.[6] This approval was based largely upon the randomized Phase 3 clinical trial, Archway[7], in which NJRetina vitreoretinal surgeons were chosen to participate as investigators. The purpose of the Archway Trial was to evaluate the safety and efficacy of the PDS with ranibizumab in patients with nAMD. The study included patients diagnosed with nAMD within nine months of trial enrollment who must have received at least three prior anti-VEGF injections with documented responses with respect

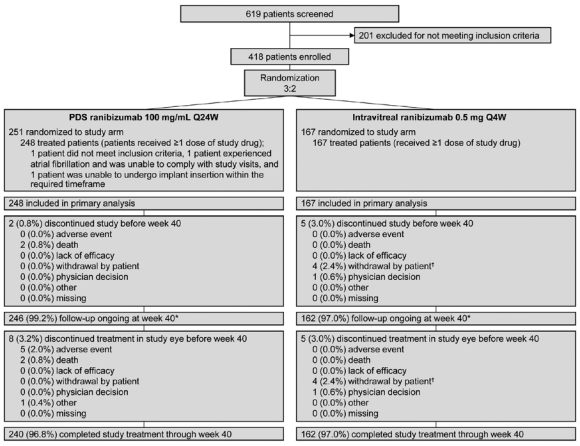

Figure 2: Archway study design, randomization, and disposition.[7]

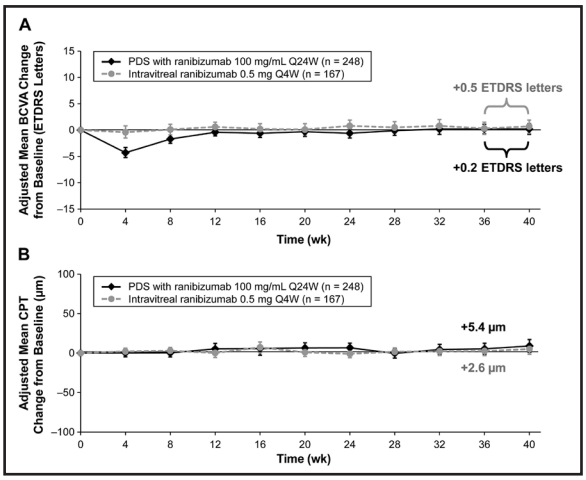

Figure 3: Graphs showing adjusted mean (A) best-corrected visual acuity (BCVA) and (B) center point thickness (CPT) change from baseline in the efficacy population.[7]

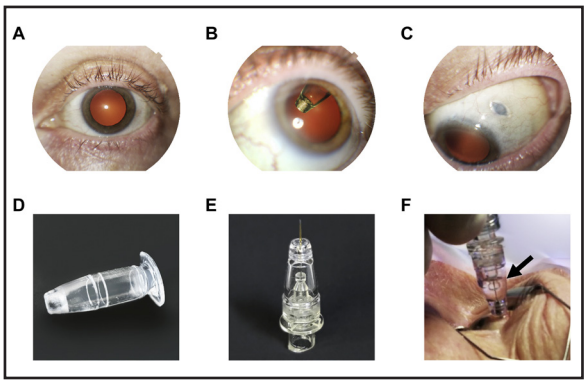

Figure 4: Port Delivery System with ranibizumab (PDS). **A–C**, Patient images from a PDS-implanted patient with **(A)** eye in primary position (implant not visible), **(B)** eye looking up with implant visible through dilated pupil, and **(C)** eye looking down to visualize PDS septum. **D, E,** Photographs showing the PDS **(D)** implant and **(E)** refill needle. F, Photograph showing the refill-exchange procedure at procedure completion with previous implant contents in the fluid collection reservoir of the refill needle (arrow). Images not at same scale.[7]

to both anatomy and vision. These study participants were randomized to receive either the PDS implant with ranibizumab and planned PDS refill at week 24 or monthly intravitreal injections of ranibizumab. The primary endpoint was change in best-corrected visual acuity at weeks 36 and 40.[7]

The Archway trial enrolled 418 patients beginning in September 2018. 251 patients were randomized to the PDS arm and ultimately 247 received the device while 167 received monthly injections of ranibizumab (Figure 2). Baseline visual acuity was balanced between the two groups and averaged Snellen equivalent was 20/32. The average change in visual acuity over weeks 36 and 40 was +0.2 ETDRS letters in the PDS group and +0.5 ETDRS letters in the injection group. Thus, the PDS met the primary endpoint of non-inferiority and equivalency to monthly ranibizumab with respect to visual acuity. There was also comparable control of retinal thickness between the two groups (Figure 3). Additionally, 98.4% of patients receiving the PDS did not require any supplemental injections during the first 24 weeks prior to the planned refill. These findings show that continuous intravitreal drug delivery resulted in similar disease control as monthly injections.[7]

Surgical Procedure and Refills

The device details and surgical procedure for implantation of Susvimo™ is detailed in the package insert.[8] Susvimo™ is an 8.4 mm permanent ocular implant that is filled with 0.02 mL (2 mg) of ranibizumab for continuous release at the time of surgical implantation and at the recommended 24-week refill interval (Figure 4). The surgical procedure takes place in the operating room using standard aseptic technique and takes approximately 45-60 minutes. The Susvimo™ implant is filled with 2 mg of 100 mg/mL ranibizumab in the operating room under sterile conditions using the provided kit. A conjunctival peritomy is made at the planned implant site, typically in the superotemporal quadrant. A 3.5 mm full-thickness scleral incision is made 4 mm posterior to the limbus until the pars plana is visible. The pars plana is then cauterized using endolaser to prevent bleeding prior to entering the eye. The incision is then carried through the pars plana into the vitreous cavity. The Susvimo™ implant is placed through this incision perpendicular to the globe using the provided inserter tool. Care is taken to orient the flanges of the device along the axis of the incision and to ensure a good fit. The conjunctiva is then meticulously closed over the implant. This step is particularly important to prevent complications such as endophthalmitis and conjunctival erosions.[7,8]

The Susvimo™ refill procedure is performed in the office under aseptic technique like that of standard intravitreal injections. Topical anesthesia is provided and the eye is sterilized with a broad-spectrum microbicide to the periocular tissue and ocular surface. The 2 mg refill dose of ranibizumab is drawn up into the Susvimo™ refill syringe and then injected into the device using a provided Susvimo™ refill-exchange needle. This needle is passed perpendicularly through the overlying conjunctiva and septum of the device and the drug is delivered over 5-10 seconds. Indirect ophthalmoscopy is performed to ensure that the device is still in its proper place and that there have been no other complications.

Cautions

Despite the promising clinical trial results and well-tolerated surgical and refill procedures outlined above, there are some cautions that ophthalmologists and patients should keep in mind when choosing Susvimo™, most notably four cases of infectious endophthalmitis in the Archway PDS arm for a rate of 2%.[7] This risk is reflected on the package insert via a boxed warning.[8] This rate contrasts sharply with commonly reported rates associated with intravitreal injections of bevacizumab, ranibizumab, and aflibercept – on the order of 1/5000 or approximately 0.02%.[9] Three out of the four cases of endophthalmitis reported in Archway were associated with conjunctival retraction, highlighting the need for meticulous closure during surgical implantation. The overall rate of conjunctival erosion in Archway was 2.4%, consistent with those found in studies of implanted glaucoma devices.[7]

Other notable complications include conjunctival blebs over the implant site and vitreous hemorrhages. Conjunctival blebs were reported in 16 patients who received the Susvimo™ implant (6.5%). Of these, 15 resolved without treatment and one required surgical revision as the implant septum could not be visualized to carry out the refill procedure.[7] Vitreous hemorrhages were reported in 13 patients who received the Susvimo™ implant (5.2%). Twelve out of the 13 occurred in the immediate post-operative period and resolved spontaneously. Of note, this rate is much improved from the earlier Phase 2 study of the PDS-ranibizumab implant in which 50% of patients experienced a vitreous hemorrhage.[10] This likely reflects an improvement in surgical technique with endolaser cautery of the pars plana prior to implant insertion.

Conclusions and Practical Application

In summary, Susvimo™ is an exciting new option for patients suffering from nAMD and retina specialists alike. Despite the need for a surgical procedure that does come with associated risks, it will likely be an attractive option for some patients – particularly those requiring frequent intravitreal injections or those with difficulty tolerating them. Like any new surgical procedure, it is reasonable to expect a learning curve both for individual surgeons and within our specialty as we work to maximize safety with this new device. To this end, Genentech is rolling out a comprehensive educational program including modules and hands-on training to get new vitreoretinal surgeons familiar with the procedure. Additionally, there is always the concern of cost for patients, physicians, and surgical centers. Genentech recently released an access and reimbursement guide to address this aspect.[11] Susvimo™ is an exciting new option for patients suffering from nAMD, as well as for the eyecare community tasked with treating them.

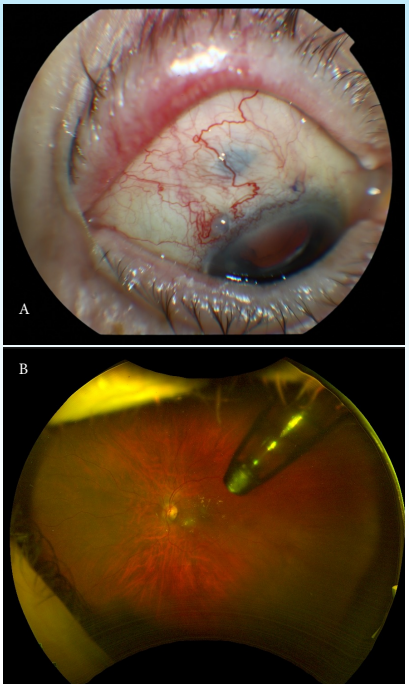

Figure 5: Color photos showing well-positioned Susvimo™ implant as viewed externally with septum visible subconjunctivally (A) and as imaged using wide-field fundus photography (B).

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At the forefront of clinical research

NJRetina continuously conducts clinical trials at key locations. Our clinical research coordinators will be happy to discuss the inclusion/exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

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Enrolling Studies:

Dry AMD

Teaneck and Toms River

Gallego: A Phase II, Multicenter, Randomized, Single-masked, Sham-controlled Study to Assess Safety, Tolerability, and Efficacy of Intravitreal Injections of FHTR2163 in Patients with Geographic Atrophy Secondary to Age-related Macular Degeneration (Gallego)

Diabetic Retinopathy

Teaneck

Altitude: A Phase 2, Randomized, Dose-escalation, Observation-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of RGX-314 Gene Therapy Delivered Via One or Two Suprachoroidal Space (SCS) Injections in Participants with Diabetic Retinopathy (DR) without Center Involved-diabetic Macular Edema (CI-DME) (ALTITUDE)

Wet AMD

Edison

Opthea Coast: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Toms River

Opthea Shore: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Teaneck

Daylight: A Two-arm, Phase 3 Study to Evaluate the Efficacy and Safety of Intravitreal KSI-301 Compared with Intravitreal Aflibercept in Participants with Neovascular (Wet) Age-related Macular Degeneration.

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