Radiation Therapy for Age-Related Macular Degeneration

Two investigational devices are designed to provide targeted delivery of radiation to reduce damage to the optic nerve and surrounding tissues.

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Radiation therapy has been evaluated extensively as a treatment for choroidal neovascularization (CNV) due to age-related macular degeneration (AMD) because of its antiangiogenic, antifibrotic, and anti-inflammatory properties.[1-3] Historically, radiation for AMD has been delivered with two broad approaches: (1) radiotherapy with external beam (megavoltage x-rays, proton beam) and (2) brachytherapy with radioactive isotopes (strontium-90, palladium-103).[4-11]

Clinical studies of external beam radiation in neovascular AMD have produced mixed results, leaving retina specialists undecided about whether it is a viable treatment option. Because the delivery of external beam radiation is not localized, it has limited ability to target only affected cells without collateral damage to healthy tissue. Low-dose beta radiation inhibits angiogenesis and has been used in the treatment of ocular tumors.[12]

The effects of radiation on neovascularization are usually delayed, sometimes by several months. During this period, the choroidal neovascular membrane can continue to grow and cause retinal damage, leading to a reduction in visual acuity before the radiation effect begins. Due to its time-of-onset limitation, radiation for wet AMD is ineffective as a monotherapy in the majority of patients.

TARGETED DELIVERY

Two companies, NeoVista, Inc. (Fremont, CA), and Oraya Therapeutics, Inc. (Newark, CA), are evaluating technologies designed to provide more targeted delivery of radiation. The Vidion Anti-Neovascular (ANV; NeoVista) therapy system utilizes a surgically inserted device to deliver intraocular exposure of radiation to the macula with strontium-90 in an epiretinal plaque brachytherapy technique over leaking blood vessels that affect central vision without causing damage to surrounding tissues. The IRay system (Oraya) is an investigational, stereotactic, radiosurgical device that uses a noninvasive, robotically controlled platform to deliver low-energy x-rays.

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EPIMACULAR BRACHYTHERAPY

In epimacular brachytherapy, a three-port pars plana vitrectomy allows the Vidion ANV to deliver beta radiation. The Vidion ANV comprises a strontium-90 source within an endoscopic probe that is held over the AMD lesion for approximately 4 minutes and then removed from the eye. According to the company, the Vidion ANV is designed to deliver targeted beta radiation to leaking blood vessels that affect central vision without causing damage to surrounding tissues. The treatment delivers the highest dose (24 Gy) to the center of the lesion, but the optic nerve receives only 2.4 Gy and the lens 0.0006 Gy. Stronium-90, with the proper dose rate and fractionation, enables epimacular brachytherapy with the Vidion ANV to deliver high doses of radiation to treat the lesions without causing damage to the surrounding tissues.

ROBOTICALLY-CONTROLLED X-RAY IRRADIATION THERAPY

The IRay system is designed to deliver low-energy x-rays precisely and reproducibly to the macula of patients with wet AMD in an office-based setting. According to Oraya, treatment planning with the IRay includes an A-scan ultrasound for axial length and the optic disk edge-to-fovea center distance. To limit radiation exposure to the optic nerve, patients with an optic disk edge-to-fovea center distance greater than 3 mm are ineligible for treatment.

When treatment is initiated, the robotically controlled device moves the x-ray point source 150 mm from the plane of the macula following a predetermined offset directly over the macula. Three 3.5-mm beams are introduced through the inferior pars plana at the 5-, 6-, and 7-o'clock positions. Each beam consists of 5.33 Gy at a distance of 150 mm from the point source. The beams overlap precisely on the macula to achieve a single 4-mm spot of total dose (16 Gy).[13] A lid speculum pulls the lower eyelid out of the path of radiation. The I-Guide (Oraya) suction-based contact lens system ensures that any eye movement is accounted for in the treatment. Less than 1 Gy is delivered to the optic nerve.[13]

CLINICAL TRIALS

NeoVista is currently conducting three clinical trials—MERLOT, MERITAGE, and CABERNET—in which epimacular brachytherapy with the Vidion ANV is performed in patients with AMD. Preliminary observations of MERITAGE suggest that a single procedure of epimacular brachytherapy reduced patients' need for ongoing anti-vascular endothelial growth factor (anti-VEGF) therapy, indicating that the Vidion ANV system may potentially reduce the burden of treatment in these resource-intensive patients while maintaining good visual outcomes.[14] Additionally, 63% of patients showed some improvement in visual acuity, with 50% gaining at least five letters at 6 months.[14] The 12-month results of CABERNET are expected to be available early next year.

More than 60 patients have been treated in a phase 1 study of the IRay device, and results from that trial led to the initiation of a masked, sham-controlled phase 3 study designed to demonstrate the efficacy and safety of radiation therapy for wet AMD. The phase 3 clinical trial is being conducted at seven European sites and will include a minimum of 150 patients previously treated with ranibizumab (Lucentis, Genentech) or bevacizumab (Avastin, Genentech), with approximately one-third of patients receiving sham treatment and the remainder receiving traditional radiation dosing with the IRay system.

CONCLUSION

Currently, neither therapy is approved by the US Food and Drug Administration for use in humans in the United States. Results of large clinical trials, as well as outcomes following approval, will be important to determine what long-term effects may exist with these novel radiation delivery systems for patients with AMD. ■

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