Exudative AMD brachytherapy trial halted but procedure could still hold promise for other indications

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A CLINICAL trial of palladium-103 (Pd-103) brachytherapy (TheraSight System; Theragenics Corporation) for the treatment of exudative age-related macular degeneration (AMD) was prematurely terminated after results fell short of the outcomes being achieved with intravitreal ranibizumab (Lucentis, Genentech), reported investigators at the annual meeting of ARVO.

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“The success of ranibizumab for stabilising and improving vision in the ANCHOR and MARINA clinical trials has raised the bar for new AMD treatments, and so Theragenics, the sponsor of this study, decided not to pursue FDA approval for its device as a monotherapy approach for AMD. Nevertheless, the experience in this clinical study supports the conclusion that the device and this minimally invasive procedure offer a safe and viable approach for local delivery of high-dose radiation to the posterior segment of the eye,” said G Baker Hubbard MD, an investigator in the study and assistant professor of ophthalmology, Emory University, Atlanta, GA.

The system has a potential role in multimodality treatment of AMD or for treating other ocular conditions amenable to radiotherapy, such as retinal or choroidal haemangioma, retinoblastoma, or other tumours. Future studies investigating those applications seem justified, he stressed.

The exudative AMD study planned to enrol 30 patients who would be randomised to receive 12, 14 or 16 Gy of radiation delivered at a prescription point 2.0mm from the face of the radiation source. Sixteen patients were enrolled before the study was terminated.

The participants had active subfoveal disease that could be classic and/or occult and measured up to 7.5mm in greatest linear dimension. Baseline vision for the 16 eyes ranged from 20/80 to 20/640.

Initial follow-up visits were scheduled on days one, seven, and 30 after the procedure, and then at less frequent intervals for three years. Currently, 11 patients are still being followed at five of the six original participating clinical centres.

Investigator assessment through indirect ophthalmoscopy and ultrasound imaging confirmed that the device could be effectively placed and correctly positioned. All patients were seen at 30 days. Fifteen patients reached the 90-day follow-up visit when the primary outcome measure for the study - development of any serious, anticipated, related adverse events - was to be assessed. Fourteen patients were seen at six months or later.

The procedure was well tolerated and the safety analysis showed the development of a single serious adverse event in a treated eye.

“Thirteen patients experienced a total of 22 non-serious adverse events. Five patients withdrew from the study, but none because of adverse events.

The goal in developing the brachytherapy system was to design a platform for administering radiotherapy in an optimal fashion with an ideal isotope in a procedure that could be performed by ophthalmologists in an outpatient setting. As previous studies of radiotherapy for exudative AMD suggested better results could be achieved using higher doses delivered with fewer fractions, the treatment was developed to deliver the radiation in a single fraction but at a high dose rate to the target tissue, which for AMD consists of the new choroidal blood vessels in the subretinal space.

Vision outcomes through last available follow-up showed that after excluding the patient who lost six lines of vision, visual acuity was stable (within 15 letters of baseline) in 14 patients and improved by more than 15 letters in one patient.

The ocular brachytherapy system consists of a sealed Pd-103 source on the distal end of an insertion applicator, a sterile sheath, and an articulating arm. The applicator with the protective sheath surrounding the radiation source is inserted via a conjunctival peritomy into the retrobulbar space and aligned flush with the sclera behind the macula. Lights on the source wand are used as a guide for positioning. Once the device is properly placed, it is stabilised by the articulating arm, and the protective sheath is withdrawn to expose the radiation source for treatment. The device delivers low energy x-rays of 21-23 keV at a high dose rate to the target tissue, which for AMD consists of the new choroidal blood vessels in the subretinal space.

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