Visit us online at www.MedPageToday.com

A | A | A | A

Drug Bests Laser for Preemie Eye Disorder

By Nancy Walsh, Staff Writer, MedPage Today
February 16, 2011

MedPage Today Action Points

- Explain that the use of bevacizumab (Avastin) for the treatment of retinopathy of prematurity appears better than conventional laser therapy.

- Note that bevacizumab is a vascular endothelial growth factor inhibitor that was initially approved for use in advanced colon cancer and which has also been used for ocular diseases such as age-related macular degeneration.

Review

The use of bevacizumab (Avastin) for the treatment of retinopathy of prematurity appears better than conventional laser therapy -- and may be a significant advance in a disease that often leads to childhood blindness, results of a prospective study showed.

The study of 150 infants found that those treated with intravitreal injections of bevacizumab had a recurrence rate in combined retinal zones I and II of 6% compared with a 26% recurrence rate in those who had conventional laser therapy (OR 0.17, 95% CI 0.05 to 0.53, *P*=0.002), according to Helen A. Mintz-Hittner, MD, and colleagues from the University of Texas in Houston.

For zone I, a circular area surrounding the optic disk, alone the recurrence rate also was higher for conventional laser therapy (42% versus 6%, OR 0.09, 95% CI 0.02 to 0.43, *P*=0.003), the investigators reported in the Feb. 17 issue of the *New England Journal of Medicine.*

For posterior zone II alone, however, the rate of recurrence did not differ, Mintz-Hittner and co-authors noted.

Retinopathy of prematurity occurs mainly in low-birth-weight infants and is a leading cause of childhood blindness worldwide.

The disease is characterized by initial episodes of hyperoxia and then hypoxia, resulting in altered levels of vascular endothelial growth factor (VEGF).

Bevacizumab is a VEGF inhibitor that was initially approved for use in advanced colon cancer, and which has also been used for ocular diseases such as age-related macular degeneration.

To assess its efficacy in retinopathy of prematurity, Mintz-Hittner and colleagues conducted a multicenter clinical trial termed BEAT-ROP (Bevacizumab Eliminates the Angiogenic Threat of Retinopathy of Prematurity) that compared bevacizumab with laser therapy in 150 infants with stage 3+ disease.

Intravitreal bevacizumab was administered in doses of 0.625 mg in 0.025 mL of solution.

Among the 143 surviving infants, there was an absolute difference of 20 percentage points in risk of recurrence (95% CI 9 to 32), the investigators found.

Reported complications were one case of corneal opacity and three cases of lens opacity -- all in the laser therapy group and in infants with zone II posterior disease.

Recurrences of retinopathy occurred bilaterally in two infants in the bevacizumab group, and retinal detachment developed in two eyes.

Recurrences were found in four infants bilaterally and in one unilaterally after laser therapy, but there were no cases of retinal detachment.

Five children in the bevacizumab group and two in the laser group died, with the most common causes being respiratory failure and low oxygen levels.

In comparing the two treatments, the investigators noted that bevacizumab is inexpensive and can easily be administered at the bedside, while laser therapy requires special equipment, facilities, and training, and also necessitates endotracheal intubation.

In addition, laser therapy often results in a significant loss of the visual field, they explained.

Mean time to recurrence in six of the eyes in the bevacizumab group was 16 weeks, while time to recurrence in 32 eyes in the laser group was 6.2 weeks.

"This serves as a warning to clinicians that careful follow-up is needed in infants treated with intravitreal bevacizumab, who cannot be considered to be successfully treated until there is completion of vascularization with no active disease or clinically significant tractional elements," Mintz-Hittner and colleagues cautioned.

They called for further research to determine the optimal doses for different stages of retinopathy and to establish follow-up requirements.

In an editorial accompanying the study, James D. Reynolds, MD, of the University at Buffalo in New York, stated, "As compared with conventional laser therapy in treating

patients with zone I retinopathy of prematurity, intravitreal bevacizumab represents a true breakthrough in disease management."

Reynolds stressed that the timing of bevacizumab treatment is of utmost importance.

If given too early, the drug could interfere with the normal vascularization of the retina, but if administration is delayed the result could be retinal detachment, he explained.

"A thorough knowledge of the pathophysiology is essential to adequately time injections," he wrote.

Increasing experience with VEGF inhibition for the retinopathy of prematurity should help clarify its indications and contraindications.

"In the meantime, intravitreal bevacizumab should become the treatment of choice for zone I retinopathy of prematurity," Reynolds concluded.

The lead investigator has acted as consultant for Bascom Palmer Eye Institute and Clarity Medical Systems. She has also provided expert testimony in a retinopathy of prematurity suit and has received fees from Pediatrix for speaking about bevacizumab.

The editorialist has been paid as an expert witness in trials involving retinopathy of prematurity and receives royalties for the glaucoma chapter in UpToDate.

Primary source: New England Journal of Medicine
Source reference:
Mintz-Hittner H, et al "Efficacy of intravitreatl bevacizumab for stage 3+ retinopathy of prematurity" *N Engl J Med* 2011; 364: 603-615.

Additional source: New England Journal of Medicine
Source reference:
Reynolds J "Bevacizumab for retinopathy of prematurity" *N Engl J Med* 2011; 364: 677-678.