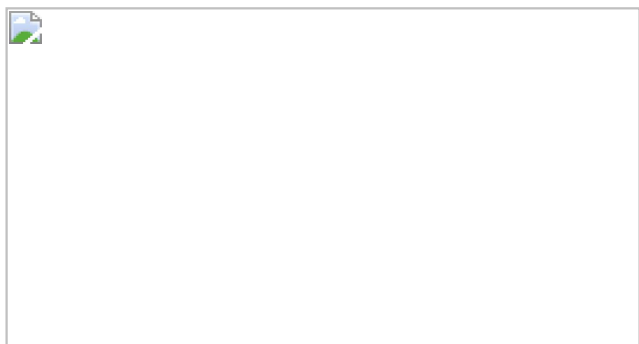


# A Cheap, Targeted Treatment for Retinopathy of Prematurity

Published Feb 16, 2011 - Written by Ishani Ganguli



Newborns who emerge too early face a world of problems.

One of these is the propensity for retinal blood vessels to grow amuck in response to erratic biochemical signals; these vessels can bleed and scar, leading to retinopathy of prematurity (ROP) – a major cause of childhood blindness in the developed and developing worlds.

Ophthalmologists usually treat ROP with laser therapy to ablate the abnormal blood vessels and the cells that produce the primary biochemical culprit: vascular endothelial growth factor (VEGF). But this approach works only about half of the time and laser treatment destroys peripheral vision.

As NEJM Deputy Editor Elizabeth Phimister notes, “It’s a very distressing condition [and] conventional laser

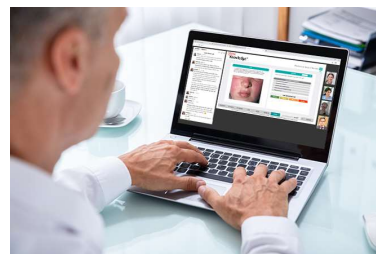
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therapy has been far from an ideal treatment.”

So why not directly inhibit VEGF? Bevacizumab is a humanized monoclonal antibody that does just that. Soon after it was approved to arrest new blood supplies to colon cancer metastases in 2004, doctors began using the inexpensive, easily administered drug off-label to treat a neovascular condition similar to ROP: age-related macular degeneration. Case series have suggested that it works for ROP, but now we have more definitive proof.

In a prospective multi-center trial reported in *NEJM* this week, researchers from the University of Texas Health Science Center at Houston randomized 150 infants with posterior, stage 3+ ROP in zones 1 and 2 to receive either the standard confluent laser therapy (CLT) or an intravitreal injection of bevacizumab (IVB) in each eye. Stage 3+, defined by prominent new blood vessels growing between the vascular and avascular regions of the eye (the + indicates the vessels are twisted), may be the optimal time for treatment—after VEGF has promoted normal vascularization and before the vessels have formed fibrous bands that would permanently disrupt the retina. The zone refers to the concentric region of retina affected (zone 1 disease includes the optic nerve and is the hardest to treat). The researchers’ primary goal in this federally sponsored study was to prevent recurrence of ROP in one or both eyes before 54 weeks postmenstrual age.

Four of the infants in the IVB group had recurrences—macular dragging or dropping—in a total of 6 eyes (4.3%), compared to 19 infants in the standard treatment group, in a total of 32 eyes (21.9%). The researchers found a significant benefit in Zone 1 retinopathy, with 6% recurrence in the IVB group compared to 42% in the laser therapy group, and a

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benefit that did not reach significance in Zone 2 retinopathy, with 5% recurrence in the IVB-treated population and 12% in the laser-treated group. They also noticed, consistent with previous reports, that the peripheral retinas of infants treated with IVB continued their normal development a year after treatment, while those of infants given CLT were definitely damaged by the treatment.

The authors caution that they were not able to evaluate safety in a trial of this size, and bevacizumab is a biologically active molecule. The authors also explain that recurrence in IVB-treated patients occurred after 4 months on average, compared to about one and a half months in CLT recipients, and so urged clinicians to monitor treated patients closely over time.

Despite the cautions, this approach promises progress against the damage done by retinopathy of prematurity. In an accompanying editorial, James D. Reynolds from the Ross Eye Institute at the University of Buffalo writes, “As compared with conventional laser therapy in treating patients with zone I retinopathy of prematurity, intravitreal bevacizumab represents a true breakthrough in disease management.”

### Questions:

What are other potential therapeutic uses of a VEGF inhibitor?

What safety concerns would you think about with systemic spread of bevacizumab in a newborn?

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