**The INCUBATOR**

Journal Club Notes:

BEAT ROP

**Title: Efficacy of Intravitreal Bevacizumab for Stage 3+ Retinopathy of Prematurity**

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**Journal: NEJM**

**Background**

In the pathogenesis of ROP, phase II or vasoproliferative phase is characterized by an increase in circulating retinal VEGF levels that stimulates the proliferation of new blood vessels, which is one of the characteristics of severe retinopathy. For this reason, using an anti-VEGF drug blocks or inhibits the production of this mediator, preventing the formation of new blood vessels. The first reports of anti VEGF use came out in 2007-2008 and showed very promising results in small patient population. In a report from Mexico published in 2008 by Quiroz-Mercado et. al. in 13 patients with ROP (18 eyes) Bevacizumab lead to regression in 17/18 eyes. Such encouraging results led to the THE BEAT ROP TRIAL (See JC NOTE).

* **What’s the question?**

Is bevacizumab better than laser therapy in patients with Strage 3+ ROP who have Zone 1 and 2 posterior disease.

* **Is it a valid question?**

Yes. Based on the pathophysiology of ROP and early report of Bevacizumab use, a large prospective trial is valid.

**Methods:**

* **Study design:**

Prospective randomized stratified controlled multicenter clinical trial

Babies, not eyes, were randomized to treatment interventions.

* **Inclusion criteria:** Infants with a birth weight of 1500 g or less and a gestational age of 30 weeks or less were examined, beginning at 4 weeks’ chronologic age or 31 weeks’ postmenstrual age, whichever was later.

Infants with stage 3+ retinopathy of prematurity in zone I or zone II posterior in each eye were eligible.

* **Exclusion criteria:** Infants with stage 4 or 5 retinopathy of prematurity in either eye were not eligible
* **Intervention:** laser therapy, compared the efficacy of intravitreal bevacizumab monotherapy (0.625 mg in 0.025 ml of solution)
* **Primary Outcome:**

treatment failure: the recurrence of neovascularization in one or both eyes arising from the retinal vessels and re- quiring retreatment by 54 weeks’ postmenstrual age (with ascertainment performed between 50 and 70 weeks). The primary ocular outcome, recurrence of retinopathy of prematu- rity, is a variable with three possible values: 0 for recurrence in neither eye, 1 for recurrence in one eye, and 2 for recurrence in both eyes

* **Secondary Outcomes:**

**Results:**

* **Baseline characteristics:** They enrolled a total of 150 infants with stage 3+ retinopathy of prematurity — 67 infants with zone I disease and 83 infants with zone II posterior disease. A total of 75 infants were randomly assigned to undergo intravitreal bevacizumab monotherapy, and 75 to conventional laser therapy
* **Primary outcome:**

The rate of recurrence (primary outcome) for **zone I and posterior zone II** combined was significantly high- er with conventional laser therapy than with intravitreal bevacizumab (26% [19 of 73 infants]) vs. 6% [4 of 70 infants]; odds ratio with bevacizumab, 0.17; 95% confidence interval [CI], 0.05 to 0.53; P = 0.002).The absolute difference be- tween the two groups in the risk of recurrence was 20 percentage points (95% CI, 9 to 32).

The rate of recurrence with **zone I disease alone** was significantly higher with conventional laser therapy than with intravitreal bevacizumab (42% [14 of 33 infants] vs. 6% [2 of 31 infants]; odds ratio with bevacizumab, 0.09; 95% CI, 0.02 to 0.43; P = 0.003

The rate of recurrence with **zone II posterior disease alone** did not differ significantly between the laser-therapy group and the bevacizumab group (12% [5 of 40 infants] and 5% [2 of 39 in- fants]; odds ratio with bevacizumab, 0.39; 95% CI, 0.07 to 2.11; P = 0.27)

* **Secondary outcomes:**

REVASCULARIZATION: Conventional laser therapy resulted in permanent destruction of the vessels in the peripheral retina, whereas intravitreal bevacizumab allowed for continued vessel growth into the peripheral retina, a finding that is consistent with previous studies of case series.

* **Other interest results**

Study was not powered to assess whether avastin was associated with higher mortality. They would have needed ˜˜3000 patients.

**Study takeaways:**

Intravitreal bevacizumab monotherapy, as compared with conventional laser therapy, in infants with stage 3+ retinopathy of prematurity showed a significant benefit for zone I but not zone II disease. Development of peripheral retinal vessels continued after treatment with intravitreal bevacizumab, but conventional laser therapy led to permanent destruction of the peripheral retina. This trial was too small to assess safety.