

TREATMENT OF ROP WITH ANTI-VEGF THERAPY: A CHILEAN PERSPECTIVE

Management of this pediatric disease requires consideration of multiple factors.

BY PAOLA DORTA S., MD, MHA, AND ANDRÉS KYCHENTHAL B., MD



The landmark CRYO-ROP study described therapeutic approaches to treating patients with retinopathy of prematurity (ROP) almost 30 years ago,¹ and since that time significant improvements have been made. In

our own ROP program in Santiago, Chile, we have recognized that conventional therapy (ie, laser photocoagulation) is not effective in some patients with posterior ROP. Even in cases in which there is a favorable anatomic result, functional outcomes may be poor due to the destructive nature of the laser treatment. This can be seen mainly in posterior zone I cases, in which vascular retinal development does not often reach the macular area. The availability of an alternative to destructive laser therapy, in the form of VEGF-inhibiting agents such as bevacizumab (Avastin, Genentech), has therefore been a boon for the management of ROP. This article describes some of our considerations in the use of anti-VEGF therapy in patients with ROP.

USING ANTI-VEGF THERAPY IN PATIENTS WITH ROP

We started using bevacizumab in the treatment of ROP 10 years ago, first in a group of patients who had progression of disease despite laser treatment, and then in babies with posterior zone I disease without macular development. In these cases, we did not laser the area where the macula should develop, but instead injected bevacizumab after performing photocoagulation.

We subsequently used bevacizumab as first-line therapy to treat type 1 ROP with a single intravitreal injection. In this series, all eyes showed regression of disease with no need for additional intervention.² Vascularization of the retina after regression of the ROP followed a normal but

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slower pattern. There was no retinal destruction and better refractive outcomes than with laser.

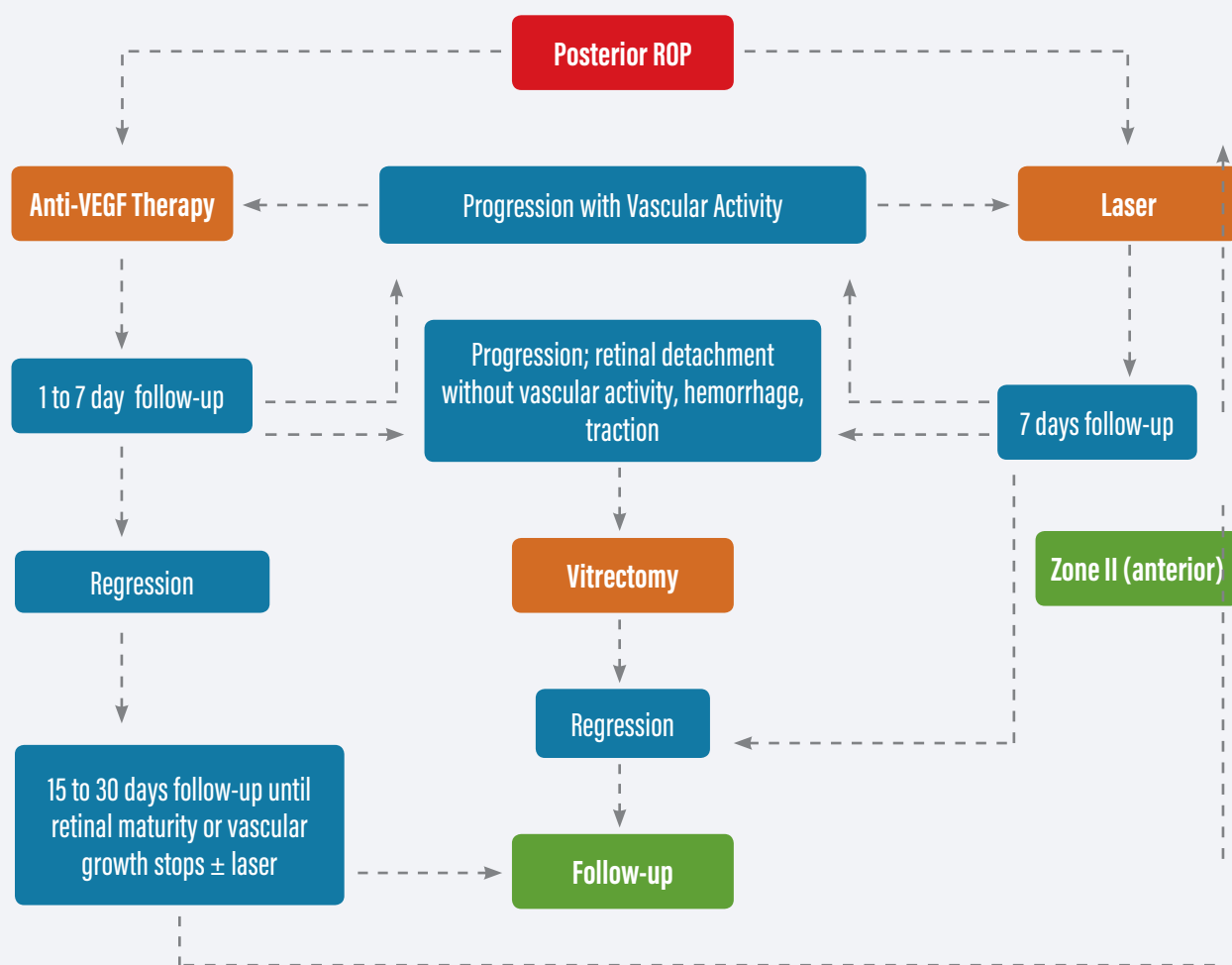
There are important issues to consider with the use of anti-VEGF drugs. Systemic safety is a significant concern, particularly in infants. We have used both bevacizumab



AT A GLANCE

- Vascular activity is a major problem in patients with RD in ROP who require surgery.
- Injection of an anti-VEGF drug before vitreoretinal surgery is recommended when vascular activity is noted in patients with RD in ROP.
- Anti-VEGF therapy may not be the best option for all patients with ROP requiring treatment.

CURRENT MANAGEMENT OF PATIENTS WITH ROP



Anti-VEGF Therapy

- Posterior ROP
- Post type 1
- Rubeosis iridis
- Vitreous haze
- Too sick for laser

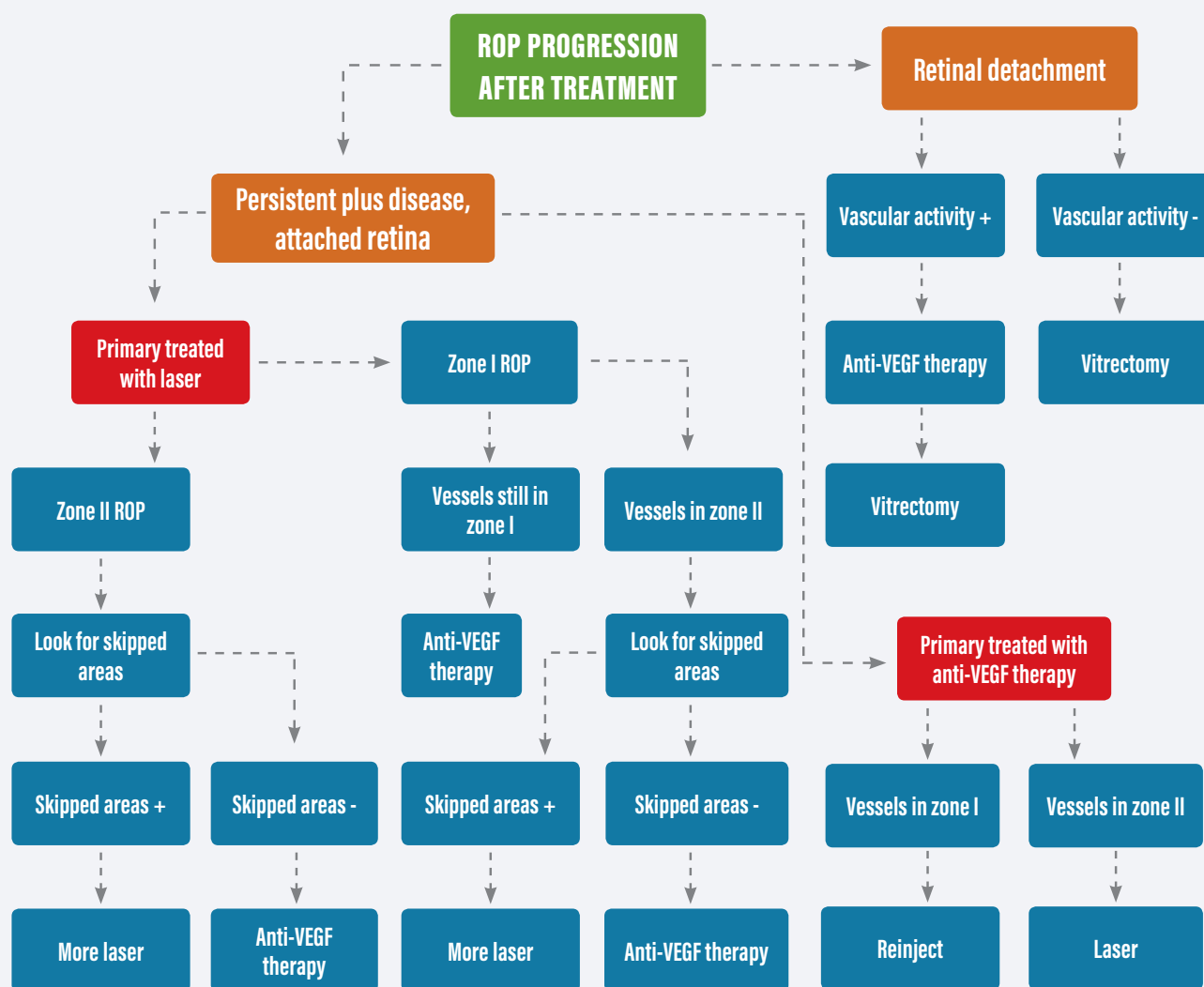
Anti-VEGF Therapy + Vitrectomy

- RD with vascular activity

Vitrectomy

- Traction
- Hemorrhage
- RD, no vascular activity

CURRENT MANAGEMENT OF PATIENTS WITH PROGRESSIVE ROP



and ranibizumab (Lucentis, Genentech) in treatment of ROP with good results.

Questions remain regarding the need for retreatments. It is our recommendation that, if there is progression of disease after the use of an anti-VEGF drug and the vessels are already in zone II, then laser therapy should be applied.

DEALING WITH RETINAL DETACHMENT

Anti-VEGF therapy has two roles in the setting of retinal detachment (RD) in ROP: 1) It can be used as an adjunct in treating RDs, *but* 2) it can cause RDs when used to treat type 1 ROP.

We performed a study to evaluate the use of an anti-VEGF agent in eyes with ROP RDs. When we injected bevacizumab 1 week before we performed vitrectomy, we observed a significant reduction in vascular activity 1 week after vitreoretinal surgery with excellent results.³

There are two types of RD that can occur due to the use of anti-VEGF drugs in the treatment of ROP. In the first type, the RD develops shortly after injection when the therapy is given too late and there is already significant traction on the retina. This has been called *ROP crunch*. The second type of RD can occur with delayed onset after the use of an anti-VEGF drug, despite an initial regression. Following these children after injection, in order to identify progression and recurrence of disease, is critically important.

Of course, anti-VEGF therapy may not be the best solution for all ROP requiring treatment. In our current management strategy for patients with ROP, we consider the use of anti-VEGF drugs as primary treatment in posterior ROP and as an adjunct in progressive disease (see “Current Management of Patients With ROP” on page 61).

Vascular Activity

Vascular activity is a major problem in patients with ROP RD who require surgery. Ideally we want to operate on an eye with no vascular activity, but delaying surgery to allow the eye to spontaneously become quiet can lead to progression of the RD. If vascular activity is noted, injection of an anti-VEGF drug 1 week before vitreoretinal surgery is recommended. The vascular regression induced by anti-VEGF therapy will allow surgical intervention to be performed in a quiet eye but without the risk of the RD progressing.

MANAGING PROGRESSIVE ROP

We base our management of patients with progressive disease on three factors: primary treatment, zone of disease, and stage of disease (see “Current Management of Patients With Progressive ROP” on page 62).

If there is persistent plus disease and no RD in an eye treated with laser for zone II ROP, treatment of skipped

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areas should be completed. If adequate treatment was given, the use of an intravitreal anti-VEGF drug is advisable.

If the eye had zone I ROP and was initially treated with laser, secondary treatment would depend on the zone where the vessels are located. If vessels are still in zone I, the injection of an intravitreal anti-VEGF drug can be performed. If vessels are in zone II, more laser should be applied if skipped areas are found.

If the primary treatment was performed with an anti-VEGF agent and there is progression with no RD present, the zone where the vessels are located will determine the secondary treatment. If retinal vessels are still in zone I, a reinjection of anti-VEGF drug may be more suitable. If vessels are in zone II, then laser photocoagulation seems to be the best alternative. It is worth noting that the patterns of regression and recurrence after the use of anti-VEGF therapy to treat ROP are not well known. This should be considered to avoid unnecessary retreatments. If progression of the disease produces an RD, the eye’s vascular activity should be evaluated to determine subsequent therapeutic actions. ■

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