# LET'S TALK ADJUNCTIVE THERAPY FOR GLAUCOMA


When do you consider adding a second drop?

BY MATTHEW D. BOVENZI, OD, FAAO, DIPL(ABO), AND RICHARD J. MADONNA, MA, OD, FAAO

A topical medication, usually a prostaglandin analogue dosed once per day, is the most common initial treatment for patients with ocular hypertension and glaucoma. Although some clinicians view the need for additional therapy as treatment failure, the need for adjunctive therapy is common and is characteristic of the progressive nature of this disease. In clinical trials, 40% or more of enrolled patients have required the use of two or more medications to maintain their target IOPs.[1,2]

When should you consider adding a second drop to a patient's treatment regimen? Read on to find out.

## DECISIONS, DECISIONS

When determining whether to add a second drug to a patient's existing treatment regimen, you first need to ask yourself whether adjunctive therapy of any kind is needed. If the answer is yes, then the next step is to figure out which *type* of adjunctive therapy is best for your patient (Figure).

## Does the Patient Need Adjunctive Therapy?

Consideration of additional IOP-lowering therapy occurs under one of two conditions: the patient's IOP is not at the target pressure that you have set, or progression is detected on structural and/or functional testing.

### Target Pressure Not Met

Establishment of a target pressure range is an essential but often overlooked element of initial glaucoma treatment. Target pressure is defined as the IOP at which further glaucomatous damage is unlikely to occur. Although the establishment of a target pressure is in part an educated guess by the provider, it should be based on the baseline untreated IOP, disease severity, and risk factors that increase the patient's chance of progression.

Following the treatment regimens of landmark studies such as OHTS[3] and CIGTS,[4] an appropriate starting point for target IOP might be 20% to 30% lower IOP than baseline for

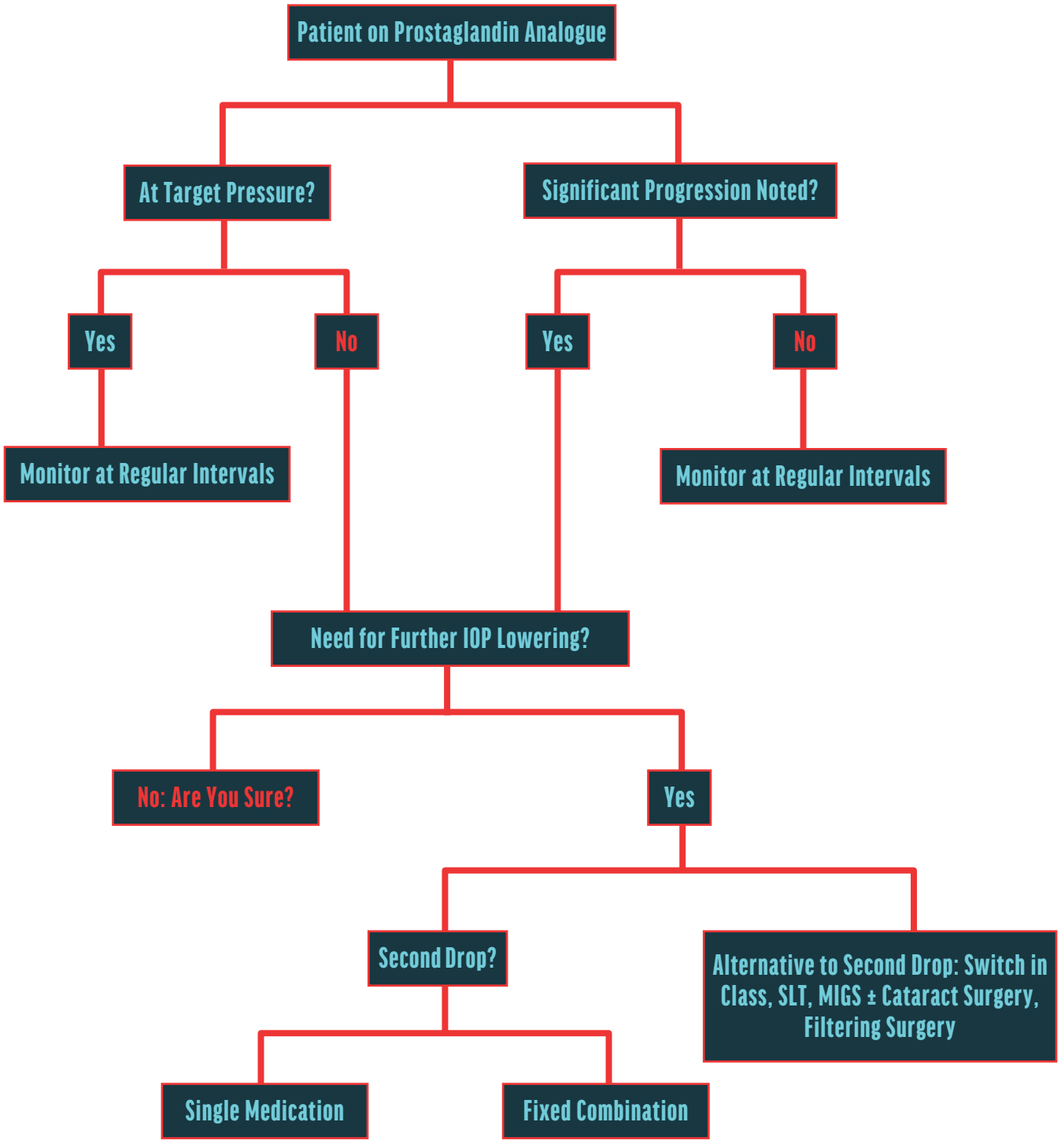


Figure. Decision tree for adding a second drop.

patients with mild glaucoma, about 30% to 40% lower for patients with moderate glaucoma, and about 40% to 50% lower for patients with severe glaucoma.

## Case Example

Consider Mr. M, a 60-year-old man of African descent whose mother had moderate glaucoma. His initial examination reveals moderate glaucomatous optic neuropathy, retinal nerve fiber layer (RNFL) thinning on OCT imaging, and corresponding visual field loss in each eye. His untreated IOP averaged over three visits is 22 mm Hg

OD and 20 mm Hg OS. Because of the severity of his disease, his age, race, and family history, you believe that a 40% decrease in IOP is indicated, so you set your target pressure at 12 mm Hg to 14 mm Hg OD and 11 mm Hg to 13 mm Hg OS.

You start Mr. M on a prostaglandin analogue and monitor him. After three follow-up visits his average pressure is 16 mm Hg OU. Adjunctive therapy should be instituted to achieve target pressure *unless* you feel that the higher IOP is acceptable for the patient, in which case your target IOP could be raised. In this case, however, given all the risk factors noted above, that would probably be unwise.

## Structural and/or Functional Progression

The most important aspects of glaucoma management include identification of structural progression, whether by disc photos or, more commonly, OCT imaging; or functional progression by analysis of sequential visual fields. Even more important is the identification of patients with rapid progression that poses a significant risk of causing loss of vision-related quality of life (VR-QOL). Rapid progression can be defined as a reduction of greater than ~2 µm per year on global RNFL thickness[5] or greater than 2 dB per year on visual field mean deviation,[6] but these are just two of many published guidelines. Such guidelines should always be considered in the context of the patient's age, severity of disease, location of field defect, and frequency of testing. When in the practitioner's judgement VR-QOL is threatened, more aggressive treatment should be instituted regardless of whether the patient was at his or her target IOP or not.

## Case Example

Mrs. G is a 68-year-old White woman with moderate glaucoma. She is being treated with latanoprost ophthalmic solution 0.005% (generic) every night at bedtime OU, which has lowered her IOP from 22 mm Hg OD pretreatment to her target IOP of between 14 mm Hg and 16 mm Hg. Recent OCTs and visual fields have both shown rapid, repeatable progression. It was felt that the rapidity of progression and her relatively young age put her at risk for loss of VR-QOL, so her target IOP was reduced to the low teens mm Hg and adjunctive therapy was instituted.

## Is a Second Drop the Best Choice for This Patient?

The answer to this question should be individualized for every patient. Alternatives to adding a second drop include laser trabeculoplasty, microinvasive glaucoma surgery (MIGS) procedures alone or with cataract surgery, or, in severe cases, glaucoma filtering surgery. The most propitious choice can be made when we take into account the patient's attitudes and comprehension of his or her disease, recognition of ocular and systemic risk factors, and knowledge of the severity and stability of his or her glaucoma, along with the risks and benefits of each adjunctive alternative. For example, laser trabeculoplasty and MIGS procedures reduce the need for adding a medication and eliminate the subsequent side effects and reduction in therapy adherence associated with adding a second drop. That said, many patients may fear laser and surgical procedures and prefer adding a second topical medication to undergoing a more invasive procedure.

## Which Drop?

After determining that a medication is the best option for your patient, you must then decide *which* to use. As with all decisions in glaucoma management, this should be individualized for each patient. There may be times when an adjunctive medicine can be avoided and the once-per-day regimen preserved by switching drugs within the prostaglandin class,

## AT A GLANCE

- Additional IOP-lowering therapy should be considered when a patient's IOP is not at the target pressure or when progression is detected on structural and/or functional testing.
- The decision to add a medication to the treatment regimen of a patient with glaucoma or ocular hypertension should be based on the patient's disease staging, risk or evidence of progression, and ability to be compliant with adjunctive therapy.
- There may be times when an adjunctive medicine can be avoided by switching drugs within the prostaglandin class, switching to a prostaglandin with a dual mechanism of action, or switching to a prostaglandin/Rho-kinase inhibitor fixed-combination drug.
- The use of multiple drops can result in ocular surface disease, but this can be managed with the use of nonpreserved artificial tears or preservative-free versions of certain drugs.

switching to a prostaglandin with a dual mechanism of action or switching to a prostaglandin/Rho-kinase (ROCK) inhibitor fixed-combination. Any of these options may provide increased IOP-lowering.

Adjunctive therapy outside the category of prostaglandin analogue can be single medications or fixed combination drops. Single medications include beta blockers, alpha-2 agonists, carbonic anhydrase inhibitors (CAIs), and ROCK inhibitors. Fixed combinations contain two medications in one bottle.

One advantage of adjunctive therapy with a single agent is the knowledge that IOP reduction or side effects are most likely due to the new medication. Generally, the IOP-lowering effects of any of these agents added to a prostaglandin analogue are similar; the chief differences between them are their side effects, dosing, cost to the patient, generic availability, nighttime efficacy, and mechanism of IOP-lowering. Each of these factors should be examined in every case.

In the past few years, use of fixed-combination medications has greatly increased.[7] In the United States, combinations of beta blockers with CAIs or alpha agonists, alpha agonists and CAIs, and most recently a ROCK inhibitor with a prostaglandin analogue are available. Fixed combinations are indicated when a patient is already taking two drops and needs further IOP lowering or when it is felt that adding a single agent will not lower the IOP adequately. Fixed combinations reduce the number of instillations, reduce drop washout, and provide excellent IOP lowering. Recently, many practitioners have gone directly to fixed combinations rather than the step-by-step addition of single medications[7] because of the excellent IOP lowering of the combination and the fact that the side effects of the individual components are well known. Cost can be a drawback, although generic formulations are available in some cases.

Importantly, the use of multiple drops can result in ocular surface disease due to the toxicity of the preservatives, chiefly benzalkonium chloride, used in some medications. Although this can be managed with nonpreserved artificial tears and other dry eye therapies, preservative-free versions of timolol and of dorzolamide HCl/timolol maleate ophthalmic solution (Cosopt PF, Akorn) are available. Additionally, the patient's prostaglandin could be switched to a preservative-free alternative or one with a milder preservative.

## WEIGHING THE OPTIONS

The decision to add a medication to the treatment regimen of a patient with glaucoma or ocular hypertension should be based on the patient's disease staging, risk or evidence of progression, and ability to adhere to adjunctive therapy. Side effects, contraindications, cost, and dosing schedule are all considerations in choosing an appropriate single-use or combination medication. If adjunctive therapy with medication is not enough or not appropriate for a given patient, whether due to compliance, cost, or other reasons, options such as laser trabeculoplasty, cataract surgery with a MIGS procedure, or filtration surgery should be explored. ■

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**MATTHEW D. BOVENZI, OD, FAAO, DIPL(ABO)**
- Assistant Clinical Professor and Assistant Chief of Primary Care, University Eye Center at the SUNY College of Optometry, New York, New York
- mbovenzi@sunyopt.edu
- Financial disclosure: None

**RICHARD J. MADONNA, MA, OD, FAAO**
- Professor and Chair, Department of Clinical Education, SUNY College of Optometry, New York, New York
- rmadonna@sunyopt.edu
- Financial disclosure: None