# The Consequences of CATT

How the study results have affected my treatment approach for AMD.

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The 1-year results of the CATT confirmed that bevacizumab (Avastin, Genentech) and ranibizumab (Lucentis, Genentech) were equivalent in terms of visual improvement regardless of whether a monthly injection schedule or an as needed (prn) schedule was used in patients with neovascular age-related macular degeneration (AMD).[1] Prior to this trial, physicians offered both drugs for the treatment of AMD; however, patients were informed that 1 drug was approved for this indication by the US Food and Drug Administration (FDA) while the other was being used off-label. Physicians could merely state that although the 2 drugs appeared to have equivalent efficacy, no direct comparison had been performed.

Now, armed with the results of the CATT, physicians have more data to provide to patients when presenting treatment options. The CATT outcomes may not have sweeping effects in determining which patient should receive which drug; however, these data, when shared with patients, may provide us with more choices. Ultimately, each patient and each eye should be examined individually in order to provide optimal care.

## BEFORE CATT

Before the CATT, I would discuss both ranibizumab and bevacizumab as treatment options for patients with AMD. I would tell patients that, in my experience, the 2 medications were essentially equivalent; however, I would also inform them that 1 of the drugs is FDA-approved for use in AMD and the other is a drug labeled for treatment of several types of cancer that would be used off-label for AMD. Additionally, I would discuss ranibizumab clinical trial data with patients. Then, after a thorough examination and testing, the patient and I would decide on the treatment based on the information I provided.

Being in private practice, my patients tend to be better educated about their treatment options, and referring physicians have generally prepared them ahead of time. Prior to the CATT, most patients in my practice preferred ranibizumab, mainly due to its FDA approval status. In academic medicine, for the most part, patients are likely to choose whichever option their doctor says is best. In private practice, however, patients tend to have stronger opinions, and it is important to educate them about their options. A drug that has FDA approval for a given indication also carries a significant amount of weight due to the implied safety profile. Because we did not have clinical trial data concerning bevacizumab's use for AMD, many patients and referring physicians generally preferred ranibizumab.

## AFTER THE RESULTS

The publication of the 1-year CATT has affected the discussion I have with my patients concerning their treatment options. Instead of telling them that no data are available for bevacizumab in AMD, I now tell them specifically about the CATT. First, I inform patients that both drugs have been used in the eye for several years. Then, using terms patients can understand, I tell them that a well-designed and executed multicenter trial compared the 2 treatments, and it found them to be equivalent in terms of efficacy. Although bevacizumab does not have FDA labeling for AMD, I think the CATT has now made it equivalent to ranibizumab in most patients' minds.

In addition to efficacy, I discuss the drugs' safety concerns to ensure that patients understand that both the efficacy equivalence and safety aspects are important. If the patient's general health is good, I do not feel there is much difference between the 2 drugs in terms of safety. On the other hand, if the patient has unstable hypertension, brittle diabetes, or heart disease issues, it may be advisable to steer toward ranibizumab based on the CATT findings.

How significantly have the CATT results affected my treatment patterns? No dramatic shift has occurred in my practice. All treatments are still individualized. Patients are switched to other options if their primary option is not achieving optimal results. However, the wider acceptance of bevacizumab after CATT likely has increased patient acceptability of the drug, thus increasing its use by 10% to 15%.

## POTENTIAL CONCERNS

In August 2011, the FDA issued a statement alerting health care professionals that repackaged bevacizumab had caused a cluster of *Streptococcus endophthalmitis*

infections. These outbreaks were concerning, as endophthalmitis is a potentially devastating complication associated with intravitreal injections. However, due to the fact that this was not a universal or general problem, these events did not affect my use of bevacizumab vs ranibizumab.

One patient in my practice referred to a report he had read concerning the possible increased risk of infection associated with bevacizumab. Following that encounter, I decided to discuss this limited outbreak with patients receiving bevacizumab. Patients were asked if they had any fears concerning the safety of the drug and if they had any questions. If necessary, patients were informed that this was likely an isolated series of events, did not occur in our area, and was not suspected to be nationwide. Most patients trusted my judgment and were maintained on their therapeutic regimens.

## AFLIBERCEPT

Recent FDA approval of aflibercept (Eylea, Regeneron) for use in neovascular AMD has prompted many inquiries by patients who are excited about the prospect of fewer injections with equivalent efficacy. Although I now include aflibercept in the initial discussion of treatment of exudative AMD along with bevacizumab and ranibizumab, I continue to encourage the use of bevacizumab or ranibizumab during the initiation phase of treatment until the lesion has stabilized. Currently, I reserve aflibercept for treatment failures of bevacizumab or ranibizumab and for patients who need maintenance therapy after a successful initiation phase of treatment. With greater physician experience and more favorable data, the use of aflibercept will likely increase. If aflibercept demonstrates comparable efficacy to these 2 anti-VEGF medications, it will likely change the landscape further in terms of exudative AMD treatment.

Important questions to be answered in the next few years include: How will the introduction of aflibercept affect the use of bevacizumab and ranibizumab? Will aflibercept be a better option than the currently employed treat-and-extend strategy? In CATT, prn bevacizumab and ranibizumab compared favorably with monthly treatment; how will aflibercept compare with these results, as it is administered bimonthly? How will long-term aflibercept safety data compare with bevacizumab and ranibizumab safety data?

## DISCUSSING OPTIONS

Patients must be counseled about several issues during their first visit. First, they should be informed of their diagnosis and prognosis. Next, they must be individually counseled about the choices of treatment. Part of this process involves counseling the patient about issues concerning their insurance coverage. Cost can be a significant factor in this discussion, and the physician's office must be aware of possible financial assistance available. The patient should also be counseled about the fact that most patients require multiple injections, often for a year or more. All patients should be told the risks, benefits and alternatives of such treatments.

Regardless of whether the patient is being treated in an academic setting or private practice, a significant amount of time should be spent with the patient and his or her family members. Exudative AMD affects the entire family. In my practice, I always discuss the diagnosis and treatment options with every patient prior to determining his or her individualized treatment protocol. In many academic institutions, several individuals are involved, and sometimes the ophthalmologist steps in to administer the injection. That method works in those environments, but in private practice we must be more hands-on with the patient-doctor relationship.

## CONCLUSION

As physicians, we spend a significant amount of time explaining diagnosis, prognosis, and treatment options for exudative AMD. Discussing clinical trial data comparing these options, their costs, and which treatment is best for the individual patient is imperative. The patient should be made aware of the treatment plan and timeframe based on factors such as lesion size, lesion characteristics, and visual acuity.

This discussion will become more complicated with newer treatment options and more clinical data. But these are exciting developments. The CATT study has changed this discussion by providing physicians with more information through a multicenter, randomized trial. This trial, and comparable ones in the future, will be invaluable in changing and improving this treatment paradigm. ■

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1. The CATT Research Group. Ranibizumab and bevacizumab for neovascular age-related mascular degeneration. *New Engl J Med.* 2011;364:1897-1908.