CATT 5-YEAR DATA: OUR PERSPECTIVE


The CATT was a groundbreaking comparative trial that showed statistical equivalence of bevacizumab (Avastin, Genentech) and ranibizumab (Lucentis, Genentech) on visual outcome after 2 years of treatment for age-related macular degeneration.[1] National Institutes of Health (NIH) funding was not approved to extend the trial beyond 2 years, during which control of drug and dosing regimens could have been maintained; however, funding was obtained for a single 5-year follow-up evaluation. At this year's annual Association for Research in Vision and Ophthalmology meeting, Daniel Martin, MD, presented the 5-year follow-up data on patients who could be evaluated from the original 2-year trial.[2]

COMMENTARY ON OVERALL FINDINGS

The study sites did a good job tracking down most (71%) of the original CATT patients who were still alive 5 years later. Of these patients, 91% were still receiving their care at a CATT center. Interestingly, despite the slightly better visual acuity (VA) in the monthly treatment arm at 2 years, almost none of the patients continued monthly treatment in the ensuing 3 years. Furthermore, roughly a quarter of patients continued use of their originally assigned drug, but the majority of patients were receiving treatment with a drug other than their assigned drug.

A disappointing finding at year 5 was that the VA gains at years 1 and 2 were lost, with the mean VA dropping 2 lines from the end of year 2 to a level 3 letters below baseline vision. This finding is not shocking, as a decrease in VA with further follow-up has been demonstrated in other studies such as HORIZON and SEVEN-UP.[3,4] The original CATT provided an early indication that results of aggressive, as-needed (prn) treatment could approach the VA results achieved with monthly treatment when treatment was based on the presence of any fluid on optical coherence tomography (OCT) rather than on a change of 50 µm in central retinal thickness or other standards that have been used. Thus, some had hoped that patients would not have been undertreated as much as in the past.

It remains unclear whether the VA loss was related to over- or undertreatment. The variability in individual treatment requirements was demonstrated by the broad distribution of injection frequency after year 2, ranging from zero to 50 injections, with the only spike seen at zero injections (in 15% of patients). However, with the findings that 83% of patients had fluid on OCT and that lesion size grew by 50% during this 5-year follow-up interval, one might be concerned that there should have been more frequent treatments rather than fewer.[2]

Development of geographic atrophy (GA) was shown in CATT, IVAN,[5] and HARBOR,[6] to be more common with monthly treatment than with prn regimens. Clearly, GA was one of the causes of decreased VA at year 5 (the incidence of GA increased from 20% at year 2 to 41% at year 5, and to 47% in those who had been in the monthly treatment arm for the first 2 years).

FINAL THOUGHTS

The remarkable gains in VA after 2 years of either bevacizumab or ranibizumab treatment in the CATT seem to have been lost over 3 years in real-world clinical practice, the majority of which was rendered at the same sites as the original trial. This is disheartening, but further study is needed to elucidate whether this loss can be minimized or eliminated by the way we provide care. On one hand, there was evidence of increased lesion size and persistent fluid as treatment and visit frequency was reduced over these 3 years. On the other hand, there was a significant increase in GA development that could be related to more frequent treatment.

It is unfortunate that the NIH did not fund a third year of the CATT to further evaluate these processes, as well as the trending differences between the two drugs seen after 2 years. It is difficult to evaluate them at the 5-year time point, with such a mix of drugs given after the end of year 2. Would the trend toward better vision with ranibizumab have become statistically significant? Would the increased drying of the retina or the fewer systemic adverse events have lost statistical significance after 3 years of treatment? Although we will not know these answers, the 5-year data provide us with valuable information that highlights our need to better understand how we should maintain and taper off anti-VEGF treatment rather than how we initiate it. ■


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