

## **Beyond AREDS: The TOZAL Study – A Paradigm Shift in the Treatment of AMD**

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Since 2001 the accepted standard of care in treating dry Age-Related Macular Degeneration (AMD) has consisted of recommending an AREDS based nutritional supplement. Clinicians may change that recommendation with the publication of the landmark TOZAL Study which was published in the February issue of the British journal *BMC Ophthalmology*.

The TOZAL Study incorporated taurine, omega-3 fatty acids, zinc, antioxidants and lutein. With the exception of taurine, this formulation is very similar to the AREDS II formulation that is in the first year of a six-year trial. The TOZAL Study design had as a primary objective the measurement of change of Visual Acuity (VA) as measured with the ETDRS charts in subjects with intermediate dry AMD who were treated with this novel nutritional supplement. The range of best-corrected VA at baseline was 20/32-20/125, the same range of VA used in the MIRA-1 study (the MIRA-1 study was used as a “distant” control group). The study contrasted VA at baseline to VA measured under the same conditions at 6 months. Based upon other studies, it is well acknowledged that VA in a group of subjects with intermediate AMD decreases over a 6-month period and the decrease has been demonstrated to be about 1.5 lines.

Remarkably, the results of the TOZAL study revealed that more than half (57%) of the subjects in the treated group improved an average of one-half a line of visual acuity at 6 months (0.0541 logMAR). In contrast to the well known natural course of AMD that demonstrates deterioration, nearly 77% treated with the nutritional supplement improved or stayed the same and only about 23% worsened (but no worse than placebo). Hence, the TOZAL supplement formula alone in this study has altered the natural course of the progression of intermediate AMD. It is well known that the original AREDS study demonstrated that nutritional supplements reduced the progression in the treated group when compared to the placebo group by about 25% but the subjects still demonstrated progression of the disease process and lost visual acuity. The AREDS II is now underway but the results will not be available for approximately 5 years. Since the TOZAL formulation is very similar (but not identical) to the AREDS II formulation, the TOZAL results predict the eventual positive AREDS II results. Conservative clinicians may choose to wait another 5 or so years for the AREDS II results to be announced before recommending TOZAL or similar nutritional supplements. Alternatively, many less conservative clinicians may choose to treat their patients with intermediate AMD with the TOZAL formula at the present time in order to provide the additional 5 or so years of protection and perhaps even result in VA improvement in as little as 6 months.

Recent literature has also indicated that higher intake of omega-3 fatty acids is associated with decreased likelihood of having wet AMD. Omega-3 fatty acids appear to influence processes involved in the development of neovascularization – specifically DHA may protect the retina by influencing which genes turn on and off, while fatty acids overall may eventually form compounds that promote cell survival and proper blood vessel

function, reduce inflammation and maintain energy balance. Considering the cost of the recommended two-year course of monthly injections of Lucentis reaches nearly \$50,000, TOZAL vitamin therapy for AMD not only makes sense, but improves quality of life at a reasonable cost.

While the TOZAL Study specifically looked at the supplement's influence on AMD, a growing body of evidence suggests that supplements containing antioxidants, lutein, and omega-3 fatty acids may reduce the risk and positively impact other eye diseases such as dry eye syndrome, cataracts, and glaucoma.

In summary, the TOZAL Study has demonstrated statistical and clinical significance of VA improvement and/or stability for subjects with intermediate AMD who were treated with the TOZAL formulation. Furthermore, omega-3 fatty acids appear to reduce the likelihood of a patient advancing to wet AMD. These findings predict that the results of the much larger AREDS II study, to be available in approximately 5 years, will yield similar positive effects.