The AREDS2 10-year Follow-on Study:

At 10 Years, the AREDS2 Data from the NEI Continues to Support a Specific Nutrient Formulation To Help Reduce Risk of Progression To Late Age-related Macular Degeneration

THE LATEST DATA: AREDS2

In 2013, results of the National Eye Institute (NEI)-supported Age-Related Eye Disease Study 2 (AREDS2) Research Group reported the findings of the 5-year, randomized, controlled AREDS2 study. This study investigated the addition of lutein/zeaxanthin (L/Z) and/or omega-3 fatty acids to the original AREDS supplement in patients with bilateral large drusen or unilateral large drusen with late age-related macular degeneration (AMD) in the fellow eye.[1] Following this, a 5-year epidemiologic follow-up study of the AREDS2 cohort was conducted from December 1, 2012 to December 31, 2018. In June 2022, the NEI published the findings of the AREDS2 10-year follow-on study in JAMA Ophthalmology, which can be found here.

Overall, the AREDS2 study demonstrated that a supplement with specific nutrients can help reduce the risk of progression of intermediate AMD to advanced AMD as well as the progression of advanced AMD to late AMD. The newly published AREDS2 10-year follow-on study data assessed the long-term effects of replacing beta-carotene with L/Z in the original AREDS supplement and tracked the nutrients' effects on the progression from intermediate AMD to advanced AMD. Safety outcomes, including diagnosis of lung cancer, were also monitored.[1]

The AREDS2 10-year follow-on study included 3,882 participants (6,351 eyes) who either had bilateral intermediate AMD or intermediate AMD in one eye and advanced AMD in the fellow eye. In addition to receiving the original AREDS formula, participants were randomly assigned to one of four treatment groups: L/Z, omega-3 fatty acids, L/Z + omega-3 fatty acids, or no additional treatment. At the halfway point of the second 5-year follow-up, 91% of the participants reported they were taking an AREDS supplement. The AREDS2 supplements (lutein, 10mg/zeaxanthin, 2mg; zinc oxide, 80mg; cupric oxide, 2 mg; vitamin C, 500 mg; and vitamin E, 400 IU), which were recommended for daily use, were provided by mail by Bausch and Lomb.[1]

THE RESULTS: A DECADE OF DATA

When the main effects of the study design were evaluated, it was revealed that the hazard ratio (HR) for progression to late AMD when comparing those assigned to L/Z versus those not assigned to L/Z at 10 years was 0.91 (**P=0.02; Figure 1**). In the secondary randomization, when the main effect analysis of L/Z versus no L/Z was restricted only to those randomized to beta-carotene, the HR was 0.80 (P=0.003), indicating a 20% reduced risk of progression to advanced AMD at 10 years.[1]

A direct analysis of L/Z without beta-carotene vs beta-carotene alone demonstrated that L/Z is beneficial in reducing the risk of progression to advanced AMD. The comparisons of 25 mg zinc vs 80 mg zinc and no beta-carotene vs beta-carotene produced HRs of 1.04 (P=0.49) and 1.04 (P=0.48), respectively. These results indicate that the 80-mg dose included in the original AREDS formula remains beneficial, and there appears to be no statistically significant benefit of including beta-carotene.[1]

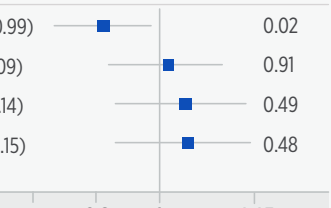
Beta-carotene has been shown to suppress serum and tissue levels of L/Z that occur naturally in the body.[2,3] In the secondary randomization, participants who were former smokers were at double the risk of developing lung cancer when receiving beta-carotene instead of L/Z. Of note, the subgroup analysis showed a stronger protective effect of L/Z over beta-carotene for progression from intermediate AMD to advanced AMD.[1]

AN ADVANCED RECOMMENDATION FOR TODAY

At 10 years, the AREDS2 study has made important strides in the understanding of how to help prevent the progression of intermediate AMD to advanced AMD and progression of advanced AMD to late AMD. The AREDS2 study demonstrated that the effects of the original AREDS formula, which has already been shown to reduce the relative risk of progression to advanced AMD by 25% over a 5-year period, are enhanced by the inclusion of L/Z, which has a relative 10% to 20% additional beneficial effect. Even the smallest chance of disease progression is meaningful to the visual lives of those currently affected by intermediate-to-advanced AMD as well as the 288 million globally projected to develop intermediate-to-advanced AMD by 2040.[4] The NEI recommends using the AREDS2 formula in all patients with intermediate-to-advanced AMD. Over 20 years of combined data can give AMD patients hope. The AREDS2 10-year follow-on study has demonstrated that the NEI-recommended formula maintains its efficacy and continues to demonstrate a favorable safety profile even after 10 years.

FIGURE 1. Analysis of Potential AREDS2 Formulation Ingredients by Main Effect[1]

	No. Eyes (No. of Events)		Hazard Ratio (95% CI)	*P*-value
Treatment	**Treatment**	**Control**		
L/Z	3180 (1475)	3171 (1565)	0.91 (0.84-0.99)	0.02
DHA/EPA	3203 (1523)	3148 (1517)	1.01 (0.93-1.09)	0.91
Low Zinc	2263 (1123)	2288 (1090)	1.04 (0.94-1.14)	0.49
Beta-Carotene	2034 (989)	2036 (997)	1.04 (0.94-1.15)	0.48



DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.

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NEI=National Eye Institute