

AREDS2: A MAJOR CLINICAL TRIAL TESTS EFFECTS OF FLORAGLO® LUTEIN ON DECREASING THE RISK OF AGE-RELATED EYE DISEASE AND IMPROVING VISUAL FUNCTION

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KEY CONCLUSIONS

- *AMD is the leading cause of vision loss among those 50 and older in the Western world.*
- *National Eye Institute, of the National Institutes of Health, initiated AREDS2 to evaluate the benefits of long-term lutein supplementation with regard to AMD, using FloraGLO Lutein.*
- *AREDS2 will also evaluate the effect of lutein supplementation on cognitive function, cataracts, cardiovascular disease, vision loss, and visual function.*

INTRODUCTION

Age-related macular degeneration (AMD) is a degenerative disease that causes progressive loss of central vision. According to the 2000 U.S. census, AMD is the leading cause of blindness for caucasian Americans over the age of 40, 54.4% cases, a figure which is expected to increase 70% by 2020 due to aging of the U.S. population (3). In fact, AMD is the leading cause of vision loss in the entire Western world among people age 50 and older (5). Presently there is no effective cure for this disease.

The Age-Related Eye Disease Study 2 (AREDS2)

The National Eye Institute of the U.S. National Institutes of Health (NIH), initiated AREDS2 as the first large randomized, double blind, placebo-controlled study to evaluate the safety and eye health benefits of long-term lutein supplementation. In June 2008, 80 participating U.S. centers completed recruitment of 4,000 AMD patients for the study with each patient receiving treatment for 5 years. Patients are randomized into four possible treatments: 10mg/day of FloraGLO® Lutein plus 2 mg/day of zeaxanthin (collectively known as xanthophylls), 1 gm/day of omega 3 fatty acids, a combined xanthophyll and omega 3 treatment, or a placebo (4). All treatments (N=3000) will be given in combination with the supplementation that was shown to be effective in the first AREDS study (Vitamin C, Vitamin E, β-carotene, zinc, and copper). See **Figure 1** for a schematic overview of the study's design.

The following is a summary of the AREDS2 ingredients along with background information regarding the study protocol.

STUDY OBJECTIVES

AREDS2 aims to refine the findings of the earlier NIH sponsored AREDS, which showed a 25% reduction in risk of progressing to advanced AMD associated with oral supplementation with high-dose antioxidants, vitamins and minerals in early AMD patients (1). AREDS2 will assess the rate of disease progression in individuals aged 50 to 85 years with advancing AMD categories 3 and 4 (bilateral large drusen, or large drusen in one eye and advanced AMD in the fellow eye). Other outcomes simultaneously to be evaluated include the effects of treatment on cognitive function, development of cataracts, cardiovascular disease, vision loss, visual function, as well as genetic risk factors to AMD.

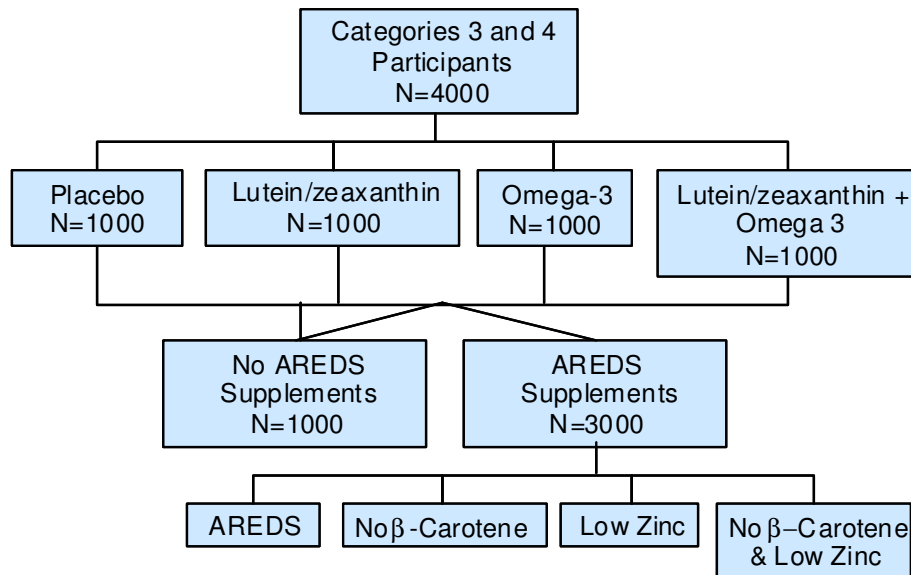


Figure 1. Graphical representation of the treatment groups that subjects will be randomized into for AREDS2.

LUTEIN DOSAGE USED IN AREDS2

Since the original AREDS trial, the body of evidence associating lutein with eye health has substantially increased. In addition to lutein, recent research linking omega 3 fatty acids to eye health has been published. Summaries of recently published studies are presented below which have been used to substantiate the need for conducting AREDS2.

Study: In 2006, Rosenthal *et al.* published a dose ranging study to examine the relationship between oral lutein supplementation and serum lutein concentration. Forty-five participants aged 60-91 without AMD, large drusen, or advanced AMD were randomized to receive one of three doses of lutein (2.5, 5, or 10 mg per day) for 6 months (9).

Results: Serum lutein levels peaked at three months with highly significant increases at all dosages at month six. Mean serum lutein concentrations from baseline to six months in the 2.5, 5, and 10 mg groups increased 2-fold (19 to 35 µg/dl), 3-fold (18 to 59 µg/dl), and 4-fold (15 to 67 µg/dl), respectively (all $p < 0.001$). No toxicity was observed during or for six months after treatment. Rosenthal demonstrated the link between increasing doses of lutein supplements and significantly increased serum levels of lutein.

Study: Khachik *et al.* (2006) investigated the distribution and metabolites of carotenoids in the serum following lutein supplementation in humans. Forty-five subjects were supplemented with one of three doses of lutein (2.5, 5.0 or 10 mg per day) for six months. Subjects were followed for six months post-supplementation for further study (6).

Results: Khachik observed a highly significant ($p < 0.0001$) increase in metabolites of lutein in serum that have previously been identified in ocular tissue. The levels of these oxidative metabolites of lutein were not correlated to dosage, likely due to their rapid reversion back to the parent molecule consistent with the mode of action of antioxidants. While serum lutein concentration gradually declined, the mean concentration of lutein metabolites remained significantly higher than baseline six months after supplementation. In this study, lutein up to 10 mg/day did not interfere with mean serum concentration including α -carotene, β -carotene, phytofluene, phytoene, lycopene, α -cryptoxanthin, and β -cryptoxanthin.

Study: Richer *et al.* published the Lutein Antioxidant Supplementation Trial (LAST) (11) in 2004. The LAST study was a double-blind, placebo-controlled trial where patients diagnosed with AMD were supplemented with FloraGLO Lutein or placebo for 12 months (8).

Results: Patients supplemented with 10 mg of FloraGLO Lutein experienced a significant increase in macular pigment optical density (36% increase, $p=0.03$ between baseline and final visit). Other parameters measured, including visual acuity and visual function, also improved in those receiving FloraGLO Lutein supplementation. The authors concluded that lutein's dual role as a blue light filter and antioxidant are likely



the reason for the observed improvements in patients.

Study: Rosenthal, Khachik, and Richer concluded independently that older individuals with and without AMD can be safely administered 10 mg of lutein for six months with no toxicity or side effects. This research was part of the fundamental evidence supporting the use of a 10 mg dosage of FloraGLO Lutein in a large long-term supplementation trial to investigate the efficacy of lutein in reducing the risk of developing advanced AMD.

Studies on Omega-3 Fatty Acids: Recent research has indicated that an increase in the consumption of omega-3 fatty acids results in a decreased risk of AMD. The most seminal research published in the area includes that from Snodderly *et al.*, Chua *et al.*, and Mitchell *et al.* (10, 2, 7). The NEI wishes to explore this putative link through the addition of omega-3 fatty acids to AREDS2.

CONCLUSION

The original AREDS study as well as other research supports the positive benefits that supplemental intervention to the diet may have in reducing the risk of progression of AMD. Research that occurred subsequent to the first AREDS study suggests that supplementation with lutein, zeaxanthin, and omega-3 fatty acids may have positive benefits on both eye health and function. AREDS2 will further build upon and strengthen the link these important nutrients have with eye health.

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