

Important Summary Facts about the Age-Related Eye Disease Study (AREDS), October, 2001

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### Study Highlights

#### **Study Description:**

- This was a randomized, placebo-controlled, double-masked clinical trial.
- 3,640 patients aged 55 to 80 years old participated in the study for AMD.
- 4,757 patients aged 55 to 80 years old participated in the study for cataract.
- Four categories of patients were followed for the AMD study:
  - Category 1 had a few small or no drusen (small (< 63  $\mu$ m) drusen in a < 125  $\mu$ m diameter circle).
  - Category 2 had several small drusen or a few medium-sized drusen in one or both eyes (small (<63  $\mu$ m) drusen in a  $\geq$  125  $\mu$ m diameter circle, or intermediate ( $\geq$  63  $\mu$ m, <125  $\mu$ m) drusen, or pigment abnormalities).
  - Category 3 had many medium-sized drusen or one or more large drusen in one or both eyes (drusen  $\geq$  63  $\mu$ m, <125  $\mu$ m drusen in a  $\geq$  360  $\mu$ m diameter circle if soft indistinct drusen are present, or in a  $\geq$  656  $\mu$ m diameter circle if soft indistinct drusen are absent, or large ( $\geq$  125  $\mu$ m) drusen, or noncentral geographic atrophy).
  - Category 4 had advanced AMD in one eye only or vision loss due to AMD in one eye only (defined as choroidal neovascularization, geographic atrophy involving center of macula, nondrusenoid retinal pigment epithelial detachment, serous or hemorrhagic retinal detachment, hemorrhage under the retina or retinal pigment epithelium or subretinal fibrosis).
- Patients received one of four treatments: 1) zinc alone; 2) antioxidants alone; 3) a combination of zinc and antioxidants; or 4) placebo.
- Follow-up time averaged 6.3 years.
- Loss to follow-up was 2.4%.
- Compliance (by pill counts) was estimated to be 75% or greater for 71% of participants. Serum levels of each of the study vitamin or mineral supplements also increased during the study period.
- 14.7% of participants had withdrawn from the study medication at end of trial.

#### **Study Results:**

*For patients with no AMD or early AMD (Category 1 and 2):*

- AREDS did evaluate treatment for patients without AMD, or patients with small drusen, pigmentary changes or nonextensive intermediate drusen, but the rate of progression to advanced AMD was too low to assess treatment effects. Thus, to date, the AREDS results demonstrated no benefits for this group. This low-risk group constitutes the majority of patients under the age of 70 years.

*For patients with intermediate AMD in one or both eyes (Category 3) and for patients with advanced AMD in one eye only or vision loss due to AMD in one eye (Category 4):*

- Patients taking a daily nutritional supplement (high-dose antioxidants and zinc) had a 20% chance of developing advanced AMD, compared to a 28% chance of developing advanced AMD for patients taking a placebo pill.

- The reduction in risk for advanced AMD for those taking the nutritional supplement (high-dose vitamins and zinc) was 25%.
- The reduction in risk for advanced AMD for those taking zinc alone was 21%, and for those taking antioxidants was 17%.
- Patients taking a daily nutritional supplement (high-dose antioxidants and zinc) had a 23% chance of developing vision loss from advanced AMD, compared to a 29% chance of developing vision loss from advanced AMD for patients taking a placebo pill.
- Results for reduction in vision loss from advanced AMD were statistically significant only for the combination of zinc and antioxidant treatment.

*For the overall group:*

- No statistically significant serious adverse effects from nutritional supplements were reported. However, hospitalizations for genitourinary disorders were more frequent for male and female participants receiving zinc.
- Nutritional supplements did not reduce the risk for progression of lens opacities or for cataract surgery.

**Study Limitations:**

- Adverse effects and toxicity over a long-term period (10 years or more) are not known.
- Individual effects of each supplement are not known.
- Nutritional supplements can help some patients, but won't protect all patients from advanced AMD, because AMD is multifactorial in nature. Some patients receiving the study medication continued to progress to advanced AMD and lose vision over time.

Study Recommendations

**Evaluation:**

- Persons over 55 years old receive a dilated eye exam to assess risk of advanced AMD.

**Treatment:**

- Patients with intermediate AMD (Category 3: extensive intermediate size drusen, or at least 1 large druse ( $\geq 125 \mu\text{m}$ ), or noncentral geographic atrophy in 1 or both eyes) and advanced AMD in one eye only (Category 4: advanced or neovascular AMD in 1 eye or vision loss due to AMD in 1 eye) should consider taking high-dose anti-oxidants plus zinc on a daily basis. The dosages used in the study were as follows: vitamin C, 500 mg; vitamin E, 400 IU; beta carotene, 15 mg (approximately 25,000 IU Vitamin A); zinc 80 mg as zinc oxide; and copper, 2 mg, as cupric oxide. Copper should be taken with zinc, because high-dose zinc is associated with copper deficiency.
- There were no benefits from treatment shown in the AREDS for patients with no AMD (Category 1) and early AMD (Category 2).

**Contraindications to Treatment:**

- Smokers and ex-smokers should not use beta carotene, because previous studies have suggested an association with lung cancer and beta carotene in smokers.

