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In Reply

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We agree with Benke and Benke that the cost of a dose-ranging study on lutein and zeaxanthin to determine efficacy for the treatment of AMD would be highly prohibitive. As they point out, it would take studies larger than AREDS2 to address the question of optimal dose. With limited resources for a large dose-ranging clinical trial, we used surrogate outcomes in smaller studies in an attempt to determine the dose of lutein we would like to test in AREDS2.[1,2] We demonstrated that oral supplementation of 10 mg of lutein resulted in a 2-fold increase in the serum level of lutein compared with baseline,[1] similar to the increases in the serum levels found using the various supplements in the original AREDS.[3] A second dosing study evaluated the serum levels after supplementation with lutein (10 mg) and zeaxanthin (2 mg) in participants randomized to lutein and zeaxanthin with or without ω-3 long-chain polyunsaturated fatty acids.[2] The resulting increases in serum lutein levels were identical in both arms. These results were replicated in AREDS2,[4] where we found a nearly 2-fold increase in the serum lutein levels in participants randomly assigned to lutein (see eTable 3 in the Supplement in the article by Chew et al[4]).

We are also aware of the issue of competitive absorption among carotenoids. In AREDS, the serum lutein levels were reduced during the study in participants randomly assigned to antioxidants that included beta carotene and vitamin E.[3] We also found a suppression of serum lutein levels in the AREDS2 participants who were simultaneously assigned to beta carotene and lutein, adjusting for serum cholesterol levels.[5] Substitution of beta carotene with lutein in the AREDS supplement alleviates this potential competitive suppression of lutein absorption.

We are gratified that evaluating our chosen lutein and zeaxanthin doses in AREDS2 provides evidence from an exploratory analysis of an incremental increase in the beneficial effect of supplements in reducing progression to late AMD, with additional analyses demonstrating this benefit only in the neovascular form of late AMD.[4,5] Additional studies would be necessary to determine whether different doses would be more or less effective.

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Conflict of Interest Disclosures: None reported.

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