



SDI Review Form 1.6

Journal Name:	Ophthalmology Research: An International Journal
Manuscript Number:	2015_OR_17131
Title of the Manuscript:	A prospective study of neuro-cognitive enhancement with carotenoids in elderly adult males with early age related macular degeneration. The ZVF Study Group (FDA IND #78,973)
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	In this manuscript, authors have studied the effects of dietary supplemental carotenoids on the cognitive skills of early AMD patients. The idea is good but unfortunately, the execution has remained very weak. Please, find specific comments below. • With these group sizes it is not possible to make comprehensive and reliable findings. Even more difficult it is to prove that the possible changes would result specifically from the studied dietary supplements. Moreover, cognitive tests alone are not enough for measuring the effects. At least the plasma levels of supplements should be controlled. In addition, if oxidative stress or the antioxidative capacity of dietary supplements became discussed, at least some supportive data should be shown.	Thank you for this review The authors state in the abstract (lines 22-24) that this is not a comprehensive study such as AREDS or AREDS 2: See lines 22-24 “Additional larger scale RCTs is indicated to investigate the clinical utility of this carotenoid in nutritional neuroscience” A larger study would involve Thousands of patients, and millions of dollars. However the methodology and statistics are sound. Yes-- We have added the following sentence (lines 133-135) Macular pigment is a well known surrogate marker of plasma levels – more so as it represents



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	• Abstract needs clarification with abbreviations opened and explained. • The symptoms of the patients should be reported. In addition, justifications specifying the early state of AMD should be clearly stated, i.e. what were the premises for AMD being regarded as early but not advanced form? Ethical statements should be reported.	end organ tissue accumulation of carotenoids following competition within the duodenum for absorption as well as lipoprotein segregation within the liver. Yes – see lines 8-16 Yes, and referenced on lines 107-108 – “as determined by a retinal specialist using the AREDS 1 simplified scale. [1]”
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<u>Minor</u> REVISION comments	• Page 2: Age-related macular degeneration has first been abbreviated as “ARM” but from the line 47 onwards, “AMD” is being used. The latter should be preferred already from the beginning. • Page 3, lines 84-85: The sentence containing “MCI” and “AD” should be rewritten. • Page 4, lines 129-133: RBANS is reported to be meant for adults aged 20-89. However, the age range of study people seems to be 54-93 (page 4, line 146). Please, explain. • Age and other characters of study subjects should be presented in Materials and Methods, not in the statistics chapter.	The word AMD in line 39 and 44 has been inserted as shown in red. Correct sentence grammar inserted in red. Correction, inserted ‘for adults age 20 and older.’ Repositioned – see lines 125-6
<u>Optional/General</u> comments	• The authors seem to realize the weaknesses of this study. The "strenghts", unfortunately, do not compensate the defects.	Yes, and the result is modest. However, we nonetheless assert this paper is important, technically sound, and the largest ophthalmologic and neurocognitive data (to date) in AMD patients taking high dose zeaxanthin.