Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Original Research Article

Post-marketing surveillance study to compare the efficacy and safety by investigating the combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc and Copper with the combination of Astaxanthin, L-Glutathione and Lutein (contains Zeaxanthin) in patients of dry age-related macular degeneration (AMD)

Lalit Pawaskar[1,*], **Amit Sharma**[1], **Mayuresh Kiran**[2]

[1] *Jagannath University, Jaipur, Rajasthan, India*
[2] *Centaur Pharmaceuticals Pvt. Ltd, Mumbai, Maharashtra, India*

ARTICLE INFO

Article history:
Received 10-07-2022
Accepted 25-08-2022
Available online 29-09-2023

Keywords:
Vitamin C
Vitamin E
Lutein
Zeaxanthin
Zinc
Copper
Astaxanthin
L Glutathione

ABSTRACT

Purpose: To determine the comparative efficacy and safety of Investigational Product – 1 (combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc and Copper) with Investigational product 2 (combination of Astaxanthin, L-Glutathione and Lutein (contains Zeaxanthin)) in patients for the indication of dry age-related macular degeneration (AMD).

Materials and Methods: It was an academic, prospective, open labelled, parallel, randomized, multicentric, comparative post-marketing surveillance study. The study was conducted at 5 clinical trial sites with 40 patients at each site. Patients with confirmed diagnosis of dry AMD in right or left or both eyes who met study inclusion and exclusion criteria were recruited for the study. The study duration was of 365 days and during the same patients were asked to visit the clinical trial site on day 30, 180 and 365 for the safety and efficacy assessment. Visual acuity, vision related quality of life and visual impairment questionnaire were the efficacy assessment parameters evaluated.

Results: Total 181 patients completed the study. It was found that there was statistically significant difference in the patients treated with the investigational product 1 and 2 for the efficacy assessment parameter, visual acuity (p value 0.0102) and vision related quality of life (p value 0.0013) and for visual impairment questionnaire score, no statistically significant difference was found (p value 0.0747).

Conclusion: Investigational product 1 was found to be more efficacious as compared to investigational product 2 for the efficacy assessment parameters visual acuity and vision related quality of life. Whereas for visual impairment questionnaire score i.e. vision required for the daily work, both products were found to be equally efficient.

1. Introduction

Age-related macular degeneration (AMD) is a common, chronic, progressive degenerative disorder of the macula that commonly affects geriatric population and majorly features loss of central vision because of abnormalities in the photoreceptor or retinal pigment epithelium (RPE) or Bruch's membrane (BrM).[1]

AMD is typically divided into "dry" and "wet" forms. Dry AMD precedes to wet AMD which is also referred as neovascular AMD, and is distinguished by choroidal neovascularization (CNV). In dry AMD the Bruch membrane (BrM) thickens, as a result of lipid and protein aggregation, which causes the development of

* *Corresponding author.*
E-mail address: lalitpawaskar@gmail.com (L. Pawaskar).

https://doi.org/10.18231/j.ijceo.2023.081

sub-RPE deposits which is isolated accumulations called drusen which may inflict stress on the RPE.[2] Dry AMD can be further classified into early, intermediate and late stages characterized by the presence of hyper and/or hypo-pigmentation with drusen within the macula.[3] The initial symptoms of dry AMD often consist of distorted vision or visual loss in the centre of the visual field. This is frequently described as stationary and centralised grey dots. In advanced stage, as the disease progresses, the disease leads to a complete loss of central vision, i.e., a central scotoma.[4] Untreated AMD and subsequent visual loss leads to poor quality of life scores, depression and restriction in daily activities.[5] 'Dry' AMD accounts for 10% of patients with visual loss.[3]

One in eight people who are 60 years or older suffer from AMD, which is the most significant cause of irreversible blindness in the geriatric population.[6–8] The prevalence of AMD was found to be 1.11% in European, 0.21% in Asian, 0.16% in Hispanic and 0.14% in African groups.[9] A systematic review was published in 2015 to determine the prevalence of AMD in Indian population which concluded that the overall prevalence of AMD in Indian patients ranges from 1.4% to 3.1%. The prevalence was found to be highest in South Indian geographical area. Also, there was a higher prevalence of early-stage AMD compared to late-stage AMD (2.3% vs 0.6%). It was found to be more prevalent in rural areas compared to urban areas. Females were more prevalent to AMD compared to males (2.3% vs 1.9%). The most important factor contributing to the prevalence of AMD was age (> 65 years).[10]

AMD is a chronic progressive condition that cannot be cured. As a result, medical measures are needed to prevent the disease from getting worse. According to research, there is no treatment for dry AMD at this point of time.[11] Dietary antioxidants, which have been shown to be effective in halting the onset and progression of AMD, are the mainstay of treatment. The retina is especially vulnerable to oxidative injury due to its high oxygen content and exposure to light. Antioxidants may be helpful in the early stages of AMD because oxidative damage is linked to the formation of drusen.[12] According to the literature there are several types of antioxidant therapies which can be utilised to delay the progression of dry AMD. These antioxidants include, but are not limited to, Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc, Copper, Astaxanthin and L-Glutathione. The macular pigment in the retina includes Lutein and Zeaxanthin which protects retina from damage caused by blue light as well as oxidative stress. Zinc and Copper are mainly responsible for antioxidative activities in retina.[13] Vitamin C as well as Vitamin E are antioxidants which prevents the development of advanced AMD as well as the loss of vision in those who already have early stage dry AMD.[14] The lens has a high concentration of Glutathione, a natural antioxidant that primarily aids in the creation of a correct image on the retina.[13] Astaxanthin is an ocular antioxidant that may help to preserve the health of the eyes.[14] The above mentioned antioxidants are available in Indian market in many combination products but out of them, for the combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc and Copper clinical trial data is available and the another is the combination of Astaxanthin, L-Glutathione, and Lutein (which contains Zeaxanthin) is widely used in India for the indication of dry-AMD. Combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc and Copper was considered as investigational product 1 for this research article and the combination of Astaxanthin, L-Glutathione, and Lutein (which contains Zeaxanthin) was considered as investigational product 2. For the purpose of comparing the efficacy and safety of investigational products 1 and 2 in Indian patients with dry AMD, a post-marketing surveillance (PMS) study was conducted. Both products were available in the Indian market.

Previously the safety and efficacy of investigational product 1 was documented during the conduct of the AREDS 2 study.[15] However, no clinical trial was carried out on Indian patients to assess the safety and effectiveness of investigational product 1 on Indian patients, also we were unable to find any clinical trial data for investigational product 2. In order to compare the efficacy and safety of investigational product 1 to 2, this was the first study conducted in India.

2. Materials and Methods

It was an academic, prospective, open labelled, parallel, multicentric, comparative PMS study to compare the efficacy and safety of Investigational product 1 with 2, in the patients of dry AMD. This PMS study was conducted at 5 clinical trial sites in India, 40 patients at each clinical trial site. Total 200 patients were recruited out of which 100 patients were randomized to investigational product 1 and 100 for the investigational product 2.

2.1. Inclusion and exclusion criteria

As per the inclusion criteria, patients of dry AMD in right or left or both eyes associated with high risk of progression to exudative AMD i.e. with drusen characteristics including soft type drusen, more than 5 drusen, drusen size greater than 63 μm ($\geq$ 5 drusen), confluence of drusen ($\geq$ 1) and retinal pigment epithelium (RPE) hyperpigmentation. Along with the same, patients of age group 50 years and above of either sex i.e. male or female, who could swallow capsule or tablet, visual acuity better than 20/200, patients agreed to stop current use of supplements containing Vitamin C, Zinc, Lutein, Zeaxanthin, Copper, Vitamin E, Astaxanthin or Glutathione other than investigational product 1 or 2 were recruited for the study. As per the

study exclusion criteria, patients with exudative AMD in the recruited eye; patients with retinal pathology other than AMD; patients with previous intravitreal injection, seizure disorder and cataract; patient with taking medication known to be toxic to the lens, retina or optic nerve; patients with chronic requirement for any systemic or ocular medication administered for other disease and known to be toxic to retina or optic nerve; patient with IOP ≥26 mmHg; patients having cataract surgery within last 3 months; patient with previous daily supplementation with 2 mg or more Lutein for period of 1 year or more prior to date of randomization; patients with Hemochromatosis; patients known to be hypersensitive to any of the excipient of the investigational products; patient who were pregnant or lactating woman excluded from the study.

2.2. Study intervention

Investigational product 1 was the fixed dose combination of Vitamin C 250mg, Zinc 40mg, Lutein 5mg, Zeaxanthin 1mg, Copper 1mg and Vitamin E 200IU per capsule. Investigational product 2 was the fixed dose combination of Astaxanthin 6mg, L-Glutathione 5mg and Lutein (contains Zeaxanthin 256mcg) 3.2mg per tablet. The subjects randomized to investigational product 1 were asked to take 2 capsules daily; 1 in the morning and 1 in the evening with food for the study duration of 365 days considering visit 1 as day 0. The subjects randomized to investigational product 2 were asked to take 1 tablet daily for the study duration of 365 days.

2.3. Study procedure

Patients of dry AMD satisfying the inclusion and exclusion criteria were recruited for the post marketing surveillance study. Information about the medical history was taken and physical examination of the eye was conducted by the investigators. Patients were either randomized to investigational product 1 or investigational product 2 by simple randomization method. Four visits were outlined for the patients recruited in the clinical trial – Visit 1 (baseline visit) on day 0, Visit 2 (well-being visit) on day 30, Visit 3 (re-evaluation visit) on day 180 and Visit 4 (conclusion visit) on day 365. Primary and secondary efficacy parameters were recorded at visit 1, 3 and 4 whereas on visit 2 only safety assessment was made. Investigators were asked to stop the investigational product in case of severe adverse event to the patient.

2.4. Concomitant therapy

There was no objection to any patient regarding any concomitant therapy but that concomitant therapy allowed were not included Vitamin C, Zinc, Lutein, Zeaxanthin, Copper, Vitamin E, Astaxanthin or Glutathione.

2.5. Efficacy assessment

Primary efficacy assessment parameter included visual acuity in each eye at visit 1, 3 and 4. The secondary efficacy assessment included the vision related quality of life and visual impairment questionnaire. Snellen chart was used to measure the visual acuity which was the primary efficacy assessment parameter. In vision related quality of life, subjects were asked to rate their overall vision related quality on a scale of 0-10, where 0 was referred as loss of vision; 1, 2 was referred as very poor vision related quality of life; 3, 4 was referred as poor vision related quality of life; 5, 6 was referred as average vision related quality of life; 7, 8 was referred as good vision related quality of life and 9, 10 was referred as very good vision related quality of life. In the efficacy assessment parameter; visual impairment questionnaire score patients were asked questions and for the same they were asked to answer the same as either no difficulty at all, a little difficulty, moderate difficulty, extreme difficulty or stopped doing this due to insufficient vision and accordingly recorded the score as 0, 1, 2, 3 or 4 respectively and by adding up the score of all 10 questions which are mentioned below, the visual impairment questionnaire score for the visit was calculated. Ten questions included how much difficulty do you have reading ordinary print in newspapers; how much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house or using hand tools; how much difficulty do you have finding something on a crowded shelf; how much difficulty do you have reading street signs or the names of stores/shops; how much difficulty do you have going down steps, stairs, or curbs in dim light or at night; how much difficulty do you have noticing objects off to the side while you are walking; how much difficulty do you have viewing movies, plays, or sports events; how much difficulty do you have doing things like shaving, styling your hair, or putting on makeup; how much difficulty do you have seeing TV/Computer/Laptops and how much difficulty do you experience while reading messages or dialling number on your mobile phone.

2.6. Safety assessment

Patients were asked for any adverse event and the same if present was recorded in the adverse event reporting form. These adverse events were classified into serious adverse events and non-serious adverse events. The adverse event was categorised as drug- or non-drug-related using WHO-UMC scale of probability.

2.7. Regulatory and ethical consideration

Ethical committee approval was taken before initiation of the study in compliance with the New Drugs and Clinical Trial Rules 2019. Both the investigational products have

been approved for manufacturing and marketing by FSSAI.

3. Results

3.1. Efficacy assessment

A total 200 clinical trial subjects were enrolled out of which 181 completed the study. Before statistical analysis of the visual acuity results, logMAR formula was applied to the value obtained from visual acuity result as converting decimal visual acuity to logMAR produces overestimation of its true value, especially in lower acuities. LogMAR value was obtained by applying the formula, logMAR= -Log(decimal acuity).[16] The total number of patients treated with Investigational Product 1 were 90 (153 eyes) whereas 91 patients (158 eyes) were treated with Investigational Product 2.

In patients treated with the investigational product 1, the mean log(MAR) value at visit 1 was 0.2684, increased to 0.2788 at visit 3 and further increased to 0.2961 at visit 4. Based on the one-way ANOVA method, there was no statistically significant increase in the log(MAR) value as the calculated F= 1.039, and the p= 0.3546. So as per the results though there was increase in the log(MAR) value it was not statistically significant. In patients treated with the investigational product 2, mean log(MAR) value at visit 1 was 0.2138, increased to 0.2243 at visit 3 and further increased to 0.3075 at visit 4. Based on the one-way ANOVA method there was statistically significant increase in the log(MAR) value as F= 20.58, and the p< 0.0001. So in patients of investigational product 2 there was increase in the log(MAR) value and it was statistically significant. In both groups, there was increase in the logMAR value but in the group of patients treated with the investigational product 2 the increase was statistically significant whereas in patients of investigational product 1 the increase was not statistically significant. When two-way ANOVA method was applied there was statistically significant difference between the group of patients treated with investigational product 1 and 2, there was statistically significant difference as p= 0.0102 and F= 4.604.

Patients treated with the investigational product 1, mean vision related quality of life at visit 1 was 6.888, increased to 6.901 at visit 3 and further increased to 7.071 at visit 4. At visit 3 and 4, the percentage increase as compared to the baseline was 0.188% and 2.656% respectively as compared to the baseline. There was no statistically significant increase in the mean vision related quality of life as p= 0.4675 and F= 0.7616. Patients treated with the investigational product 2, mean vision related quality of life at visit 1 was 7.2088, increased to 7.424 at visit 3 and at visit 4 reduced to 6.7531. At visit 3, the percentage increase as compared to baseline was 2.996% and at visit 4, percentage reduction of 6.312% as compared to baseline. To check the statistical significance of the reduction of the mean vision related quality of life at visit 4 as compared to visit 1, the one-way ANOVA method was applied and p= 0.0004, F= 7.841 which was found to be statistically significant reduction. In patients treated with the investigational product 1, there was increase in mean vision related quality of life which was not statistically significant whereas in the group of patients treated with the investigational product 2, there was reduction in the mean vision related quality of life which was statistically significant. For comparative analysis, two-way ANOVA method was applied and there was statistically significant difference found with p= 0.0013, F= 6.683.

Patients treated with the investigational product 1, mean visual impairment questionnaire score was 20.433 at visit 1, reduced to 19.022 at visit 3 and further reduced to 16.777 at visit 4. At visit 3 and 4, there was reduction of 6.905% and 17.892% respectively as compared to baseline. When one-way ANOVA method was applied, p= 0.0281 and F= 3.622 which indicated there was statistically significant reduction. In patients treated with the investigational product 2, mean visual impairment questionnaire score was 17.450 at visit 1, reduced to 16.428 at visit 3 and increased to 17.626 at visit 4. At visit 3 and 4, there was reduction of 5.856% and increase of 1.008% respectively as compared to baseline. When one-way ANOVA method was applied there was statistically significant increase as p= 0.5812, F= 0.5437. For comparative analysis, when two-way ANOVA method was applied in both the group, there was no statistically significant difference found as p= 0.0747 and F= 2.606.

3.2. Safety assessment

In patients treated with the investigational product 1, 2 episodes of adverse events were observed in 2 patients. All the adverse events observed were of non-serious nature.

Table 1: Adverse events occurred during the conduct of the study in the group of patients treated with the investigational product 1

Adverse events	No. of episodes	No. of patients
Gastritis	1	1
Continuous Hyperacidity	1	1

In patients treated with the investigational product 2, 5 episodes of adverse events were observed in 6 patients. All the adverse events observed were of non-serious nature.

Table 2: Adverse events occurred during the conduct of the study in the group of patients treated with the investigational product 2

Adverse events	No. of episodes	No. of patients
Nausea	2	2
Headache	1	1
Constipation	1	1
Bloating	1	1

4. Discussion

Dry AMD is a progressive disease responsible for blurred or decreased central vision and if left untreated then causes the loss of vision. The disease progresses over years and treatment includes only slowing the progression of the disease which includes various combinations of the antioxidants. There are so many combinations of antioxidants available in the market and this study was conducted to compare the efficacy and safety of the investigational product 1 and 2 in the Indian patients of dry-AMD.

The primary efficacy assessment was made using the visual acuity test and for secondary efficacy assessment vision related quality of life and visual impairment questionnaire score was used. A total of 90 patients completed the study who were treated with investigational product 1, i.e. 153 eyes and 91 patients completed the study who were treated with investigational product 2 i.e. 158 eyes. For visual acuity test, Snellen chart was used. In the group of patients treated with the investigational product 1, the mean log(MAR) value at visit 1 was 0.2684, increased to 0.2961 at visit 4. There was no statistically significant increase in the mean log(MAR) value as F= 1.039, and the p= 0.3546. In patients treated with the investigational product 2, the mean log(MAR) value at visit 1 was 0.2138, increased to 0.3075 at visit 4. There was statistically significant increase in the mean log(MAR) value as F= 20.58, and the $p < 0.0001$. In both group of patients, there was increase in the mean log(MAR) value but in the group of patients treated with the investigational product 2 increase was statistically significant whereas in the group of patients of investigational product 1 the increase was not found to be statistically significant. When two-way ANOVA method applied between both the group of patients, there was statistically significant difference as the p= 0.0102 and F= 4.604. So according to the results visual acuity was found to be maintained in the group of patients treated with the investigational product 1 but in the group of patients treated with the investigational product 2, the visual acuity was found to be worsened.

In patients treated with investigational product 1, the mean vision related quality of life was increased from 6.888 at baseline visit to 7.071 at visit 4. This increase in the mean vision related quality of life was not found to be statistically significant as p= 0.4675 and F= 0.7616. Whereas in patients treated with the investigational product 2, the mean vision related quality of life at baseline was 7.2088 reduced to 6.7531 at visit 4. This reduction in the mean vision related quality of life was found to be statistically significant as p= 0.0004 and F= 7.841. In patients treated with the investigational product 1, there was increase in mean vision related quality of life which was not statistically significant whereas in the group of patients treated with the investigational product 2, there was reduction in the mean vision related quality of life which was statistically significant. For comparative analysis, two-way ANOVA method was applied for the group of patients treated with the investigational product 1 and 2 and there was statistically significant difference with p= 0.0013, F= 6.683 which indicated that vision related quality of life was maintained in patients treated with the investigational product 1 whereas in patients treated with the investigational product 2, it was worsened.

In patients treated with the investigational product 1, mean visual impairment questionnaire score at visit 1 was 20.433 reduced to 16.777 on visit 4. There was statistically significant reduction in the mean visual impairment questionnaire score as p= 0.0281 and F= 3.622. In patients treated with investigational product 2, mean visual impairment questionnaire score at visit 1 was 17.450 increased to 17.626 at visit 4. The increase in the mean visual impairment questionnaire score was not statistically significant as p= 0.5812 and F= 0.5437. For comparative analysis when two-way ANOVA method was applied, between both the groups, statistically significant difference was not found as p= 0.0747 with F=2.606 which indicated, visual impairment questionnaire score i.e. visual functions were improved in the group of patients treated with investigational product 1 whereas in the group of patients treated with investigational product 2, it was found to be maintained but there was no statistically significant difference between both the groups. On assessing the safety between the 2 investigational products in this study, 2 patients among the investigational product 1 experienced adverse events. 1 patient developed gastritis and 1 patient had continuous hyperacidity. Both the patients had only one episode of adverse effects. Whereas, in patients treated with the investigational product 2, 6 patients experienced adverse events. Out of which, 3 patients developed 2 episodes of nausea, 1 patient had headache, 1patient developed constipation and 1 patient complained of bloating with only one episode. However, all the adverse events observed were of non-serious in nature. Below we have discussed studies which meets the same outcome that we have made.

Huang, Yang-Mu et al. conducted a randomized, double-blinded, placebo-controlled trial to compare the efficacy for different doses of Lutein or Zeaxanthin on serum levels, macular pigmentation and visual performance on 112 patients with early age-related macular degeneration. Group 1 (lutein 10mg), group 2 (Lutein 20mg), group 3 (combination of lutein 10mg and Zeaxanthin 10mg) or group 4 (placebo). The parameters used to ensure the efficacy were Serum Lutein/Zeaxanthin concentrations, macular pigment ocular density (MPOD), and visual performance indices including best-spectacle corrected visual acuity (BCVA), contrast sensitivity (CS), and flash recovery time (FRT) were quantified at baseline, 24 weeks, 48 weeks, and 2 years. According to the study's findings,

MPOD and serum Lutein levels were drastically increased with each active treatment. Increase in serum levels showed a statistical significant results between group 1 and 2 (P<0.05). However, none of the groups showed significant differences in BCVA or FRT during the conduct of the clinical trial. The results of the study indicated that for the first 48 weeks, the formulation with Group 2 was more effective in elevating the MPOD and CS (P<0.05), however Group 1 and Group 2 showed statistically insignificant differences (P>0.05). In groups 1, 2, or 3, there were no statistically significant changes in BCVA or FRT during the study (P>0.05). Patients with early AMD may have an improved outcome with increase in MPOD, serum Lutein concentration, and visual sensitivity with long-term Lutein supplementation.[17]

In order to examine the effectiveness of treating the patients with early or intermediate age-related maculopathy with Lutein, other antioxidants, and minerals, Wolf-Schnurrbusch Ute E. K. et al. conducted a clinical trial on 79 patients. Efficacy assessment parameters were contrast sensitivity (CS) and macular pigment optical density (MPOD). Group 1 (Lutein 10 mg, Vitamin C 60 mg, Vitamin E 20 mg, Vitamin B3 10 mg, Copper 0.25 mg, Zinc 10 mg and Zeaxanthin 1 mg) and Group 2 (Lutein 10 mg, Vitamin C 60 mg, Vitamin E 20 mg, Vitamin B3 10 mg, Copper 0.25 mg, Zinc 10 mg, Zeaxanthin 1 mg and Omega-3-fatty acid [DHA/EPA] 160 mg). Based on the study's outcomes, the levels of Lutein in group 1 showed significant increase (P= 0.005) when compared to group 2 (P = 0.059). The MPOD levels during the course of one year demonstrated a comparatively gradual decline with a significant difference between two groups (P=0.01). After 6 months, contrast sensitivity increased in group 1 (P=0.01) while being stable in group 2 (P=0.086). After six months the supplementation was stopped and the CS scores in group 1 significantly reduced, but no changes were seen in the group 2. Similarly, the plasma levels of Lutein and Zeaxanthin showed changes only in Group 1. Both the plasma concentrations of Lutein and Zeaxanthin showed a significant difference between the groups (P=0.01). This signifies that the effect of Lutein on macular pigmentation and CS was reduced and in addition of Omega acids it decreased the bioavailability of Lutein.[18]

5. Conclusion

The results concluded that the fixed dose combination of Vitamin C 250 mg, Zinc 40 mg, Lutein 5 mg, Zeaxanthin 1 mg, Copper 1 mg and Vitamin E 200 IU per capsule was found to be efficient in maintaining the visual acuity as there was no significant difference (p=0.3546) between visual acuity of baseline. Also investigational product 1 was found to be efficient in improving the visual impairment questionnaire score as there was significant reduction (p=0.0281) in the visual impairment questionnaire score but it was not found to be efficient in increasing the vision related quality of life as though there was increase in the vision related quality of life but it was not statistically significant (p=0.4675) so it can be concluded that investigational product 1 maintained the vision related quality of life. The investigational product 2, fixed dose combination of Astaxanthin 6 mg, L-Glutathione 5 mg and Lutein (contains Zeaxanthin 256 mcg) 3.2 mg per tablet was not found to be efficient in maintaining the visual acuity as there was statistically significant (p=0.0001) increase in the log(MAR) value i.e. reduction in the visual acuity at visit 4 as compared to baseline. Also, it was not found to be efficient in maintaining the vision related quality of life as there was statistically significant reduction (p=0.0004) in the vision related quality of life but at the same time as there was no statistically significant increase (p=0.5812) in the visual impairment questionnaire, the investigational product 2 was efficient in maintaining the visual functions in the patients.

During the comparative analysis between the group of patients treated with the investigational product 1 and investigational product 2, investigational product 1 was found to be more efficient in maintaining the visual acuity (p=0.0102), maintaining vision related quality of life (p=0.0013). There was no statistically significant difference (p=0.0747) found in maintaining or improving the visual impairment questionnaire score i.e. the vision required for daily activities so for that investigational product 1 and investigational product 2 were equally efficient in maintaining the vision required for daily activities.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Gheorghe A, Mahdi L, Musat O. Age-related macular degeneration. *Romanian J Ophthalmol*. 2015;59(2):74–7.
2. Bowes RC, Farsiu S, Toth CA, Klingeborn M. Dry age-related macular degeneration: mechanisms, therapeutic targets, and imaging. *Invest Ophthalmol Vis Sci*. 2013;54(14):68–80.
3. Ayoub T, Patel N. Age-related macular degeneration. *J R Soc Med*. 2009;102(2):56–61.
4. Stahl A. The Diagnosis and Treatment of Age-Related Macular Degeneration. *Dtsch Arztebl Int*. 2020;117(29-30):513–20.
5. Morris B, Imrie F, Armbrecht AM, Dhillon B. Age-related macular degeneration and recent developments: new hope for old eyes? *Postgrad Med J*. 2007;83(979):301–7.
6. Vyawahare H, Shinde P. Age-Related Macular Degeneration: Epidemiology, Pathophysiology, Diagnosis, and Treatment. *Cureus*. 2022;14(9):e29583.
7. Vanderbeek BL, Zacks DN, Talwar N, Nan B, Musch DC, Stein JD. Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network. *Am J Ophthalmol*. 2011;152(2):273–82.

8. Fleckenstein M, Keenan TDL, Guymer RH, Chakravarthy U, Schmitz-Valckenberg S, Klaver CC, et al. Age-related macular degeneration. *Nat Rev Dis Primers*. 2021;7(1):31.
9. Schultz NM, Bhardwaj S, Barclay C, Gaspar L, Schwartz J. Global Burden of Dry Age-Related Macular Degeneration: A Targeted Literature Review. *Clin Ther*. 2021;43(10):1792–818.
10. Likhar N, Mothe RK, Kanukula R, Shah C, Dang A. The prevalence of age related macular degeneration in Indian population: a systematic review. *Value Health*. 2015;18(3):180.
11. Girmens JF, Sahel JA, Marazova K. Dry age-related macular degeneration: A currently unmet clinical need. *Intractable Rare Dis Res*. 2012;1(3):103–14.
12. Chong EWT, Wong TY, Kreis AJ, Simpson JA, Guymer RH. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ*. 2007;335(7623):755.
13. Giblin FJ. Glutathione: a vital lens antioxidant. *J Ocul Pharmacol Ther Off J Assoc Ocul Pharmacol Ther*. 2000;16(2):121–35.
14. Giannaccare G, Pellegrini M, Senni C, Bernabei F, Scorcia V, Cicero AFG. Clinical Applications of Astaxanthin in the Treatment of Ocular Diseases: Emerging Insights. *Mar Drugs*. 2020;18(5):239.
15. Chew EY, Clemons T, SanGiovanni JP, Danis R, Domalpally A, McBee W, et al. The Age-Related Eye Disease Study 2 (AREDS2): study design and baseline characteristics (AREDS2 report number 1). *Ophthalmology*. 2012;119(11):2282–9.
16. Mataftsi A, Koutsimpogeorgos D, Brazitikos P, Ziakas N, Haidich AB. Is conversion of decimal visual acuity measurements to logMAR values reliable? . *Graefes Arch Clin Exp Ophthalmol*. 2019;257(7):1513–7.
17. Huang YM, Dou HL, Huang FF, Xu XR, Zou ZY, Lin XM. Effect of supplemental lutein and zeaxanthin on serum, macular pigmentation, and visual performance in patients with early age-related macular degeneration. *Biomed Res Int*. 2015;2015:564738. doi:10.1155/2015/564738.
18. Wolf-Schnurrbusch UEK, Zinkernagel MS, Munk MR, Ebneter A, Wolf S. Oral Lutein Supplementation Enhances Macular Pigment Density and Contrast Sensitivity but Not in Combination With Polyunsaturated Fatty Acids. *Invest Ophthalmol Vis Sci*. 2015;56(13):8069–74.

Author biography

Lalit Pawaskar, Research Scholar https://orcid.org/0000-0002-6437-3485

Amit Sharma, Professor https://orcid.org/0000-0002-1407-5228

Mayuresh Kiran, Vice President

Cite this article: Pawaskar L, Sharma A, Kiran M. Post-marketing surveillance study to compare the efficacy and safety by investigating the combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc and Copper with the combination of Astaxanthin, L-Glutathione and Lutein (contains Zeaxanthin) in patients of dry age-related macular degeneration (AMD). *Indian J Clin Exp Ophthalmol* 2023;9(3):425-431.