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Meso-zeaxanthin Ocular Supplementation Trial (MOST)

Submission date	Recruitment status	[_] Prospectively registered
05/09/2008	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/10/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/12/2011	Eye Diseases	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.wit.ie/mprg

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NA

Study information

Scientific Title
Macular and serum responses to supplemental Meso-zeaxanthin, Lutein and Zeaxanthin (Macushield™/MacuHealth with LMZ)

Acronym
MOST

Study objectives
Age-related macular degeneration (AMD) is the most common cause of blind registration in the western world. It is estimated that AMD affects approximately 1.4 million individuals in the United States, 417,000 people in the United Kingdom and 70,000 people in the Republic of Ireland, and this number is likely to increase due to increasing longevity. Although the aetiological mechanisms leading to AMD are uncertain, there is a growing consensus that cumulative short wavelength (blue) light damage and/or oxidative stress play a role.

The central retina, known as the macula, is responsible for central, colour and fine-detail vision. A pigment, composed of the three dietary hydroxycarotenoids, meso-zeaxanthin (MZ), lutein (L) and zeaxanthin (Z) (MZ is also formed in the retina following conversion from L), accumulates at the macula where it is known as macular pigment (MP). MP is a blue light filter and a powerful antioxidant, and is therefore believed to protect against AMD. In addition, there is good reason to believe why supplementation with MZ, L and Z would enhance a patient's retinal sensitivity.

Several studies have investigated the relationship between dietary and serum concentrations of L (and Z) and MP optical density in humans, and all have demonstrated a positive relationship between these variables. Non-dietary variables suspected of acting as determinants of serum concentrations of L (and Z) and/or MP optical density include: age; sex; iris colour; race; body fat; ultraviolet light exposure; cumulative visible light exposure; tobacco and drinking habits; and genetic background. However, the exclusively dietary origins of L and Z suggest that dietary intake (fruit and vegetables and/or dietary supplements) of these carotenoids represents one of the most important determinants of serum L (and Z) and MP optical density.

To date, there have been several published studies in the literature reporting on L and/or Z supplementation with respect to serum carotenoid and MP levels, in human subjects. In 1997, Hammond et al. showed that dietary modification, for as little as four weeks, could augment MP, with this effect being maintained for several months following resumption of a normal, unmodified diet. Of note, two of the 11 subjects involved in that study did not show a significant rise in MP optical density despite a significant increase in serum L. These subjects were termed "retinal non-responders" and this phenomenon may be due to a compromised ability to capture and/or stabilise the macular carotenoids in these individuals. Landrum et al. investigated the effect of L supplementation in two individuals over a 140 day period. They found an increase in serum L levels in both individuals, coupled with a parallel increase in MP optical density. Most recently, a study by Trieschmann et al. concluded that supplementation with 12 mg L and 1 mg Z, combined with co-antioxidants, resulted in a significant increase in MP optical density in a majority of subjects. However, there has only been one study which has investigated the effects of supplemental MZ and that study consisted of only 10 subjects and nine controls which were recruited in a non-randomised manner. MZ is a particularly interesting macular carotenoid for

the following reasons:
1. MZ is the dominant carotenoid in the central fovea: of the three macular carotenoids, MZ is the most powerful antioxidant in the presence of its binding protein
2. MZ facilitates a wider range of blue light filtration
3. At an anatomic level, MZ is more closely related to vulnerable photoreceptors than either L or Z, and is therefore ideally located to afford protection against free radical damage.

In addition, the design of all studies to date are limited, as no study has yet investigated supplementation of any macular carotenoid in subjects using a double-blind randomised placebo controlled design. Also, all supplementation studies to date have reported only on the peak MP optical density. This is a major limitation, due to the fact that most of the studies to date would have supplemented with L only, and it is known that L accumulates in the periphery of the MP and not at the centre where these measurements would have been made. In other words, it is likely that previous studies reporting on L supplementation with respect to MP levels would have missed (or were unable to detect) significant increases in peripheral MP levels. In brief, therefore, a properly designed study capable of investigating MZ, L and Z supplementation with respect to serum and MP levels (including its entire spatial profile), in human subjects is truly merited.

This study is designed to investigate (in a double-blind, randomised placebo controlled fashion) changes in MP optical density (including its entire spatial profile), and in serum concentrations of MZ, L and Z, in response to supplementation with MacuShield™/MacuHealth with LMZ (a specialised, comprehensive formula of MZ, L and Z) in normal subjects, and investigate whether MP augmentation in such subjects enhances retinal sensitivity.

Please note that, as of 21/01/2009, the public title of this trial has been amended from "Human response to Macushield™/MacuHealth with LMZ" to "Meso-zeaxanthin Ocular Supplementation Trial (MOST)". Acronym has also been changed from "MZ Trial" to "MOST".

Ethics approval required
Old ethics approval format

Ethics approval(s)
Granted by the Research Ethics Committee in the Waterford Regional Hospital, Ireland on the 11th August 2008.

Study design
Double-blind randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Patient information sheet can be found at http://www.wit.ie/mprg

Health condition(s) or problem(s) studied
Age-related macular degeneration (AMD)

Interventions
Patients were randomised to:
1. Intervention group: one tablet of Macushield™/MacuHealth with LMZ (dosage: 10 mg L, 10 mg MZ, 2 mg Z) orally, once daily
2. Control group: one tablet of placebo (rice flour) orally, once daily

The total duration of treatment was six months, the total duration of follow-up was three months.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Macushield™/MacuHealth with LMZ (Meso-zeaxanthin, Lutein and Zeaxanthin)

Primary outcome measure
MP optical density (including its entire spatial profile), as measured by heterochromatic flicker photometry [HFP].

Primary and secondary outcome measures will be carried out at baseline, three, six and nine months.

Secondary outcome measures
1. Assessment of retinal sensitivity using microperimetry
2. Serum L and Z (including MZ) concentrations as measured by high-performance liquid chromatography [HPLC]
3. Comparison of MP optical density values measured using the validated gold standard customised HFP device (Densitometer™) to MP optical density values obtained using a MP screening device (MacuScope™)

Primary and secondary outcome measures will be carried out at baseline, three, six and nine months.

Overall study start date
01/10/2008

Completion date
01/01/2010

Eligibility

Key inclusion criteria
1. Any race
2. Male or female
3. Aged 18 to 60 years
4. No presence of ocular pathology
5. Visual acuity of at least 6/18 in the study eye

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Outside age range 18 to 60 years
2. Pregnancy
3. Presence of ocular pathology

Date of first enrolment
01/10/2008

Date of final enrolment
01/01/2010

Locations

Countries of recruitment
Ireland

Study participating centre
Macular Pigment Research Group
Waterford
Ireland
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Sponsor information

Organisation
Macuvision Europe Limited (UK)

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Sponsor type
Industry

Website
http://www.macushield.com

ROR
https://ror.org/001zd1d95

Funder(s)

Funder type
Industry

Funder Name
Macuvision Europe Ltd (UK)

Funder Name
MacuHealth US (USA)

Funder Name
MacuHealth Canada (Canada)

Funder Name
Macuscope US (USA)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	29/11/2011		Yes	No