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Age-related macular degeneration Meso-zeaxanthin Ocular Supplementation trial (AMOST)

Submission date 23/01/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 27/08/2009	**Overall study status** Completed	
Last Edited 30/11/2011	**Condition category** Eye Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title
Comparison of macular and serum responses after supplementation with two different macular carotenoid formulations

Acronym
AMOST

Study objectives
Age-related macular degeneration (AMD), the late stage of age-related maculopathy (ARM), is the most common cause of blind registration in the western world. It is estimated that AMD affects approximately 1.4 million individuals in 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 ARM are uncertain, there is a growing consensus that cumulative short wavelength (blue) light damage and/or oxidative stress play a role in this disease.

The central retina, known as the macula, is responsible for central, colour and fine-detail vision. A pigment, composed of the three dietary hydroxycarotenoids, lutein (L) and zeaxanthin (Z), and meso-zeaxanthin (MZ) (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 ARM. In addition, there is good reason to believe why supplementation with L, Z and MZ would enhance a patients 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; 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. 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-randomized manner. MZ is a particularly interesting macular carotenoid for the following reasons. MZ is the dominant carotenoid in the central fovea: of the three macular carotenoids, MZ is the most powerful antioxidant; MZ facilities a wider range of blue light filtration; 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.

Given that there are many factors which affect the bioavailability and uptake of MZ, L and Z into the retina, it is possible that other commercially available products designed to augment MP, such as Macushield™, may show a more favorable response than previously tested formulations. We believe that the ideal formulation to augment MP would contain all three of the macular carotenoids (MZ, L, and Z), primarily because all other commercially available products (at least

in the context of a typical diet which does not include MZ-containing foods, such a shrimp and salmon) depends on the individuals ability to convert L to MZ within the retina, and this process may well be dependent on specific enzymatic isomerisations. In other words, MacuShield™ (because it contains MZ) is the only formulation which provides all three macular carotenoids, without the need for conversion of any of these compounds within the retina.

In addition, the design of all studies to date are limited, as no study has yet investigated supplementation of any of the macular carotenoids in ARM subjects in a double-blind randomised controlled fashion. 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 patients with ARM is truly merited and will accredit any MP product which is tested in this manner.

Furthermore, as there are now many different carotenoid-based products available on the market, with various different formulations and concentrations of the macular carotenoids, it is timely, therefore, to compare patient response (in serum and macula) to such formulations. In this way, suffers of ARM, and people at risk of developing this disease, will be informed as to which product provides the greater augmentation of serum and retinal levels of the macular carotenoids following supplementation with these compounds.

This study is designed to compare two different carotenoid-based products, in a double-blind, randomised controlled fashion, with respect to changes in MP optical density, and in serum concentrations of MZ, L and Z. This study will also investigate whether MP augmentation enhances visual performance in AMD patients.

A predecessor to this trial has been registered with an ISRCTN and can be found at http://www.controlled-trials.com/ISRCTN60816411; this previously registered trial was performed in a population of normal healthy participants where the primary outcome measure was macular and serum responses to Macushield™. This trial is designed to investigate morphological changes in age-related macular degeneration (AMD) after supplementation with Macushield™ and a lutein product.

As of 30/11/2011 the anticipated end date for this trial has been updated. The original date was 01/03/2011.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Research Ethics Committee, South Eastern Region, Ireland gave approval on the 28th November 2008

Study design
Double-blind randomised clinical trial

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact Eithne Connolly (econnolly@wit.ie) to request a patient information sheet

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

Interventions
Group 1: MZ 10 mg; L 10 mg; Z 2 mg (intervention group 1)
Group 2: 10 mg L plus an additional contamination of circa 1 mg Z (intervention group 2)

The treatment will be 12 months in duration and visits for the trial will be baseline, 3 months, six months and twelve months of supplementation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lutein (L), zeaxanthin (Z), meso-zeaxanthin (MZ)

Primary outcome measure
Measured at baseline, three months, six months and twelve months:
1. Morphological changes in AMD, with respect to baseline and between groups 1 and 2 over the study period
2. MP optical density (including its entire spatial profile), as measured by heterochromatic flicker photometry (HFP)
3. Comparison of MP optical density response between groups 1 and 2 over the study period

Secondary outcome measures
Measured at baseline, three months, six months and twelve months:
1. Serum MZ, L and Z concentrations as measured by high-performance liquid chromatography (HPLC)
2. Comparison of serum carotenoid response between groups 1 and 2 over the study period
3. Assessment of retinal sensitivity using microperimetry

Overall study start date
01/03/2009

Completion date
01/03/2012

Eligibility

Key inclusion criteria
1. Male or female, aged 50 years and above
2. Early stage AMD in at least one eye
3. No additional ocular pathology to AMD

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Cigarette smokers
2. Currently taking dietary supplements and/or had been taking dietary supplements over the previous three months prior to their baseline study visit
3. Diabetics (HbA1c above 6.5%)

Date of first enrolment
01/03/2009

Date of final enrolment
01/03/2012

Locations

Countries of recruitment
Ireland

Study participating centre
Suite 14, Whitfield Clinic
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Ireland
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Sponsor information

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Howard Foundations Holdings Limited (UK)

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Howard Foundations Holdings Limited (UK)

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