# Age-related macular degeneration Mesozeaxanthin Ocular Supplementation trial (AMOST)

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

# Plain English summary of protocol

Not provided at time of registration

# Contact information

# Type(s)

Scientific

#### Contact name

Dr John Nolan

### Contact details

Suite 14, Whitfield Clinic Butlerstown North Cork Road Waterford Ireland

+353 (0)51 302018 jnolan@wit.ie

# Additional identifiers

**EudraCT/CTIS** number

**IRAS** number

ClinicalTrials.gov number

Secondary identifying numbers

# 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 $^{\text{TM}}$ , 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

Waterford Ireland

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# Sponsor information

### Organisation

Howard Foundations Holdings Limited (UK)

### Sponsor details

Whitehill House Granhams Road Great Shelford Cambridge United Kingdom CB2 5JY

### Sponsor type

Industry

### Website

http://www.howard-foundation.com/

#### **ROR**

https://ror.org/03ywwjy69

# 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