ISRCTN82949875 https://doi.org/10.1186/ISRCTN82949875

Saponins for macular disease

Submission date 15/04/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/04/2024	**Overall study status** Ongoing	
Last Edited 02/02/2026	**Condition category** Eye Diseases	

Plain English summary of protocol

Background and study aims
Photoreceptor cells in the retina of the eye detect light and their death results in blindness. These cells are supported by the delivery of nutrients from the blood, across Bruch's membrane and the retinal pigment epithelium (RPE), and the removal of toxic waste products in the opposite direction. In the young, Bruch's membrane is fairly porous allowing an efficient exchange of nutrients and waste products, but with age, there is an accumulation of deposits resulting in a decrease in the ease with which these products are transported. In age-related macular degeneration (AMD), these ageing changes in Bruch's membrane are advanced, compromising metabolic support to the photoreceptors and leading to blindness. The obvious intervention in the disease would be to remove the deposits and restore the metabolic support to the photoreceptor cells. This study aims to establish whether treatment of AMD with oral saponins or glycoside supplements, which can remove some of the waste products from Bruch's membrane, is feasible and acceptable to participants.

Who can participate?
Patients aged 60-85 years with AMD in both eyes and early or intermediate-stage AMD in at least one eye

What does the study involve?
Participants are randomly allocated to take an oral glycoside supplement (triterpenoid saponins) or matched placebo (dummy) tablets daily after a meal for 4 months. Participants attend the optometry centre for six visits over 12 months.

What are the possible benefits and risks of participating?
There were no adverse effects in any of the many clinical trials with saponins. Rare cases of mild insomnia, diarrhoea, nausea, headache and gastric discomfort have been reported but were only transitory. Some controversy remains as to whether saponins interfere with warfarin anticoagulant treatment. Participants being treated with warfarin (and vitamin K antagonists [phenindione, acenocoumarol]) will be excluded from this trial. Breathing problems, tightness in the throat, chest pain, skin hives, rash or itchy or swollen skin may mean a participant is allergic to sea cucumber products and should stop taking them immediately. Therefore, people with a known or suspected seafood allergy cannot participate.

Where is the study run from?
Cardiff University Optometry Centre and City Sight Optometry Centre, City, University of London (UK)

When is the study starting and how long is it expected to run for?
October 2020 to September 2025

Who is funding the study?
AltRegen Co. Ltd (South Korea)

Who is the main contact?
Dr Joanna Smith, Trial Manager, Centre for Trials Research, Cardiff University, SAMADI@cardiff.ac.uk

Contact information

Type(s)
Scientific, Public

Contact name
Dr Joanna Smith

Contact details
Trial Manager, Centre for Trials Research, Cardiff University
Cardiff
United Kingdom
CF24 4HQ
+44 (0)29 20 687 904
SAMADI@cardiff.ac.uk

Type(s)
Principal investigator

Contact name
Dr Tom Margrain

Contact details
Device Chief Investigator
School of Optometry and Vision Sciences
Cardiff University
Maindy Road
Cardiff
United Kingdom
CF24 4HQ
+44 (0)29 2087 6118
margrainth@cardiff.ac.uk

Type(s)
Principal investigator

Contact name

Prof Marcela Votruba

Contact details
Main Chief Investigator
School of Optometry and Vision Sciences
Cardiff University
Maindy Road
Cardiff
United Kingdom
CF24 4HQ
+44 (0)29 20870117
VotrubaM@cardiff.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Dr Ashley Wood

Contact details
Lead Principal Investigator at lead site (Cardiff)
Cardiff
United Kingdom
CF24 4HQ
+44 (0)29 20875063
WoodA2@cardiff.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2021-003045-38

Integrated Research Application System (IRAS)
1004543

Central Portfolio Management System (CPMS)
58443

IRAS number for use with MHRA Devices outside of IRAS combined review
325909

Protocol serial number
SPON1833-20

Study information

Scientific Title
Oral glycoside supplement (triterpenoid saponins) for early and intermediate stage age-related macular degeneration: an exploratory randomised placebo-controlled trial

Acronym
SAMADI

Study objectives
To establish whether treatment of age-related macular degeneration (AMD) with oral glycoside supplements is feasible and acceptable to participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/03/2024, Health and Social Care Research Ethics Committee A (HSC REC A) (Office for Research Ethics Committee Northern Ireland (ORECNI), Lissue Industrial Estate West, 5 Rathdown Walk, Lisburn, BT28 2RF, United Kingdom; +44 (0)28 95 361400; reca@hscni.net), ref: 23/NI/0060

Study design
Multicentre double-masked individually randomized placebo-controlled feasibility trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Men and women with early or intermediate stage age-related macular degeneration (AMD) in the trial eye and any stage of AMD in the non-trial eye

Interventions
Randomisation will take place at baseline visit 2 (up to 3 weeks after baseline visit 1) when eligibility has been confirmed. Randomisation will be by blocked randomisation stratified by site and age-related macular degeneration (AMD) severity.

Oral glycoside supplement (triterpenoid saponins) versus matched placebo, 4 tablets (117 mg saponins total daily dose) daily, orally, after a meal for 4 months.

Follow up 4 months after baseline (after treatment has ended): Month 4, visit 1, followed by Month 4, visit 2 (up to 4 weeks after visit 1). Month 12, visit 1 followed by Month 12 visit 2 (up to 4 weeks after visit 1).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Triterpenoid saponins

Primary outcome(s)

The feasibility of a subsequent fully powered trial, assessed using:
1. Recruitment: the proportion of those contacted who are randomised will be tabulated to give an idea of the feasibility of recruitment into a trial in this population
2. Retention: to assess retention over 4 and 12 months. Participants will be contacted by the researchers monthly during the 4-month treatment period. Participants will be sent reminders prior to their 4- and 12-month appointments. The proportion of those randomised who provide complete follow-up clinical data at each timepoint by arm will be tabulated.
3. Adherence to treatment. Participants will be given a tablet diary to complete over the 4-month treatment period (from baseline) and will receive monthly 'compliance' phone calls from the researchers to be 'reminded' to take their medication. The diary will be returned at 4 months, visit 1. The proportion of participants who adhered to the treatment regimen will be tabulated. The proportion of tablets taken per patient will also be tabulated by arm, assessed from tablet counts.
4. Acceptability of the intervention: an end-of-trial participant questionnaire at 12 months, visit 1, to assess the acceptability of the IMP and trial procedures and for participants to be able to speak about their experiences whilst taking part in the trial
5. Feasibility of the eligibility assessment process: the proportion of participants with all required information to determine eligibility from baseline visit 1 to baseline visit 2: the time taken and the percentage of people who the researchers think are eligible, i.e. who complete baseline visit 1, but who are, on the basis of GP feedback, later ruled out from baseline visit 2 and the study
6. Feasibility of collecting the outcome data: levels of data completeness will be tabulated for each follow-up timepoint for each outcome measure with confidence intervals by arm
7. Serious adverse events (SAEs) including comparative rates between arms. The number of SAEs in each arm will be monitored and tabulated during the intervention and throughout follow up

Key secondary outcome(s))
Measured at baseline, 4 and 12 months:
1. Dark adaptation with calculation of cone tau(s), rod cone break time (s) and the slope of the S2 component of the rod dark adaptation function (log cdm-2 per s)
2. Visual acuity measured using a standard Early Treatment Diabetic Retinopathy Study (ETDRS) test in both eyes and binocularly with their distance refractive error in place (number of letters)
3. Contrast sensitivity measured using a Pelli Robson letter chart in both eyes and binocularly with participant's habitual distance refractive error in place
4. Patient-reported outcome measure (PROM) (Low Luminance Questionnaire) score
5. International Society for Clinical Electrophysiology of Vision (ISCEV) electrophysiology protocol recorded using an Espion E3 Electroretinography System. The standard ISCEV ERG protocol for both eyes includes the following individual tests: dark-adapted 0.01 ERG; dark-adapted 3 ERG; dark-adapted 10 ERG; light-adapted 3.0 ERG; light-adapted 30 Hz flicker ERG. The parameters (amplitudes and implicit times) for each test will be calculated.
6. Beckman AMD clinical grading based on colour fundus photography of the posterior pole from both eyes (45° photographs) and augmented by evaluation of optical coherence tomography macular images (20° x 20°)
7. Retinal and intra-retinal layer thickness derived from automated segmentation of optical coherence tomography macular images (20° x 20°)
8. Near infra-red confocal scanning laser ophthalmoscopy (NIR cSLO) and optical coherence tomography macular images obtained using a Heidelberg Spectralis and colour retinal photography to provide a visual record of ocular/retinal health and assess eligibility

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 25/07/2024:
1. Aged 60 to 85 years old (inclusive)
2. Able to provide informed consent and comply with the trial visit schedule
3. AMD in both eyes (of any stage)
4. Early or intermediate stage AMD (Beckman classification) in at least one eye

Previous participant inclusion criteria:
1. Aged 55 to 85 years old (inclusive)
2. Able to provide informed consent and comply with the trial visit schedule
3. AMD in both eyes (of any stage)
4. Early or intermediate stage AMD (Beckman classification) in at least one eye

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
60 years

Upper age limit
85 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current participant exclusion criteria as of 25/07/2024:
1. Ocular pathology in the study eye (or in either eye for genetic conditions or glaucoma), other than age-related macular degeneration, which may affect visual function
2. Intraocular pressure of 24 mmHg or greater
3. Grade <2 van Herick or history of allergic reaction to dilating eye drops
4. Unable to classify AMD grade
5. Lens opacity greater than grade 2 on any Lens Opacities Classification System III (LOCS III) criterion, or other media opacity/nystagmus that might interfere with quality retinal imaging
6. Diabetes
7. Vitamin A deficiency
8. Other significant systemic disease or medication known to affect visual or retinal function
9. Systemic illness that would compromise participation in a 1-year trial
10. Actively under treatment for cancer

11. Diagnosed with cancer with ocular involvement
12. Insufficient English language comprehension
13. A possible cognitive impairment as determined using an abridged Mini-Cog. This is defined as a score of less than 3.
14. Known or suspected seafood allergy
15. Photosensitive epilepsy
16. Currently treated with warfarin or other vitamin K antagonist
17. Participation in any other interventional trial within 30 days prior to entering this trial
18. Men who are planning a pregnancy with their partner or have partners who are women of childbearing potential
19. Taking supplements containing saponins (e.g. ginseng)
20. Unable to consume the IMP or placebo for a period of longer than 24 hours during the treatment window (for example a prolonged fast or repeated 24-hour fast)
21. Participants undergoing planned, forthcoming major surgical interventions

Previous participant exclusion criteria:
1. Ocular pathology in the study eye (or in either eye for genetic conditions or glaucoma), other than age-related macular degeneration, which may affect visual function
2. Intraocular pressure of 24 mmHg or greater
3. Grade <2 van Herick or history of allergic reaction to dilating eye drops
4. Unable to classify AMD grade
5. Lens opacity greater than grade 2 on any Lens Opacities Classification System III (LOCS III) criterion, or other media opacity/nystagmus that might interfere with quality retinal imaging
6. Diabetes
7. Vitamin A deficiency
8. Other significant systemic disease or medication known to affect visual or retinal function
9. Systemic illness that would compromise participation in a 1-year trial
10. Actively under treatment for cancer
11. Diagnosed with cancer with ocular involvement
12. Insufficient English language comprehension
13. A possible cognitive impairment as determined using an abridged Mini-Cog. This is defined as a score of less than 3.
14. Known or suspected seafood allergy
15. Photosensitive epilepsy
16. Currently treated with warfarin or other vitamin K antagonist
17. Participation in any other interventional trial within 30 days prior to entering this trial
18. Women who are pregnant, lactating or planning a pregnancy, or men who have a partner who is planning a pregnancy
19. Taking supplements containing saponins (e.g. ginseng)
20. Unable to consume the IMP or placebo for a period of longer than 24 hours during the treatment window (for example a prolonged fast or repeated 24-hour fast)
21. Participants undergoing planned, forthcoming major surgical interventions

Date of first enrolment
01/04/2025

Date of final enrolment
19/12/2025

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Cardiff University
Eye Clinic and School of Optometry and Vision Sciences
Maindy Road
Cardiff
Wales
CF24 4HQ

Study participating centre
City Sight, University of London
Northampton Square
London
England
EC1V 0HB

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Industry

Funder Name
AltRegen Ltd

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date