Clinical Trials in Age-Related Macular Degeneration Treatment

Jeffrey N. Weiss

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For the patients that have allowed us the privilege to serve.

Preface

This book is a compendium of the worldwide ocular stem cell, gene therapy, pharmaceutical, and other miscellaneous studies treating Age-Related Macular Degeneration registered with Clinicaltrials.gov. Clinicaltrials.gov is the largest website listing of registered clinical research studies in the world. The information presented is accurate as of November 2023. I have divided the studies into multiple categories: Completed, Active/Recruiting, Active/Not-Recruiting, Not Yet Recruiting, and Enrolling by Invitation. Regarding study location, United States locations are listed first, followed by other countries in alphabetical order. As studies have many sites, frequently in many countries, the sponsor location is used.

I corrected the mischaracterization of studies, only included those that truly belonged within each category, removed extraneous information, and corrected spelling and grammar, in order to produce a consistent and easy-to-read format. The Study and the Clinical Trial number are provided to make it easier for the reader to obtain further information.

I hope that by providing this reference, the field of age-related macular degeneration treatment will be advanced.

Parkland, FL, USA — Jeffrey N. Weiss

Contents

Chapter 1
Introduction to Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is the leading cause of visual loss in the elderly population. The hallmark of AMD is the presence of drusen, which are composed of lipids, proteins, lipofuscin granules, and small RNAs. The late stage of AMD may be divided into a "wet" or neovascular type, and the much more common "dry" or atrophic type also called geographic atrophy. Currently, there are effective treatments in the form of Vascular Endothelial Growth Factor Inhibitors, laser photocoagulation, and photodynamic therapy for patients with wet AMD, but there is no effective treatment for the dry type of AMD.

Smoking, obesity, and high-fat diets have been shown to impact the development and progression of AMD. Initially, dietary supplements, such as lutein, zeaxanthin, and omega-3 fatty acids, were shown to slow AMD progression but further analysis did not prove efficacy.

Visual cycle modulators, inflammatory modulators, and neuroprotective agents have all been studied in an attempt to slow the progression of dry AMD. Oxidative and mitochondrial stresses are postulated to promote the development and progression of AMD but no effective pharmacological interventions have proven successful.

Fifty percent of the risk of developing AMD has been explained by a complex association of genetics, environment, and lifestyle. Genetic linkage analysis has identified multiple sets of genetic variants that have roles in immune response, inflammatory processes, and retinal homeostasis.

Replacement of the retinal pigment epithelium (RPE) using cell-based therapies has been performed but this technique relies upon the presence of remaining photoreceptors. Treating significant geographic atrophy, with the loss of all the retinal layers, remains problematic. Difficulties include the formation of functional synapses, and the successful orientation and polarization of the donor photoreceptors following transplantation.

In this book, we explore the various potential therapies being evaluated in the treatment of both neovascular AMD and geographic atrophy.

J. N. Weiss, *Clinical Trials in Age-Related Macular Degeneration Treatment*,
https://doi.org/10.1007/978-3-031-58803-7_1

Further Reading

Harris JR, Fisher R, Jorgensen M, et al. CD 133 progenitor cells from the bone marrow contribute to retinal pigment epithelial repair. Stem Cells. 2009;27(2):457–66.

Gong L, Wu Q, Song B, Lu B, Zhang Y. Differentiation of rat mesenchymal stem cells transplanted into the subretinal space of sodium iodate-injected rats. Clin Experiment Ophthalmol. 2008;36:666–71.

Jiang Y, Zhang Y, Zhang L, et al. Therapeutic effect of bone marrow mesenchymal stem cells on laser-induced retinal injury in mice. Int J Mol Sci. 2014;15:9372–85.

Becker S, Jayaram H, Limb GA. Recent advances towards the clinical application of stem cells for retinal regeneration. Cells. 2012;1:851–73.

Pesaresi M, Bonila-Pons SA, Simonte G, et al. Endogenous mobilization of bone-marrow cells into the murine retina induces fusion-mediated reprograming of Müller glia cells. EBioMedicine. 2018;30:38–51.

Schmier JK, Covert DW, Lau EC. Patterns and costs associated with progression of age-related macular degeneration. Am J Ophthalmol. 2012;154(4):675–81.

Wong WT, Chakravarthy U, Klein R, Mitchell P, et al. The natural history and prognosis of neovascular age-related macular degeneration: a systematic review of the literature and meta-analysis. Ophthalmology. 2008;115(1):116–26.

Buschini E, Fea AM, Lavia C, Nassisi M, et al. Recent developments in the management of dry age-related macular degeneration. Clin Ophthalmol. 2015;9:563–74.

Cheung LK, Eaton A. Age-related macular degeneration. Pharmacotherapy. 2013;33(8):838–55.

Chew EY, Clemons TE, Agron E, Sperduto RD, et al. Age-relate eye disease study research: ten-year follow-up of age-related macular degeneration in the age-related eye disease study: AREDS report no. 36. JAMA Ophthalmol. 2014;132(3):272–7.

Suter M, Reme C, Grimm C, Wenzel A, et al. Age-related macular degeneration. The lipofusion component N-retinyl-N-retinylidene ethanolamine detaches proapoptotic proteins from mitochondria and induces apoptosis ibn mammalian retinal pigment epithelial cells. J Biol Chem. 2000;275(50):39625–30.

Baudouin C, Peyman GA, Fredj-Reygrobellet D, Gordon WC, et al. Immunohistological study of subretinal membranes in age-related macular degeneration. Jpn J Ophthalmol. 1992;36(4):443–51.

Danis RP, Lavine JA, Domalpally A. Geographic atrophy in patients with advanced dry age-related macular degeneration: current challenges and future prospects. Clin Ophthalmol. 2015;9:2159–74.

Maller J, et al. Common variation in three genes, including a noncoding variant in CFH, strongly influences risk of age-related macular degeneration. Nat Genet. 2006;38:1055–9.

Schwartz SD, Regillo CD, Lam BL, Eliott D, et al. Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase ½ studies. Lancet. 2015;385(9967):509–16.

Forest DL, Johnson LV, Clegg DO. Cellular models and therapies for age-related macular degeneration. Dis Model Mech. 2015;8(5):421–7.

Song WJ, Park KM, Kim HJ, et al. Treatment of macular degeneration using embryonic stem cell-derived retinal pigment epithelium: preliminary results in Asian patients. Stem Cell Rep. 2015;4(5):860–72.

Weiss JN, Levy S. Stem cell ophthalmology treatment study (SCOTS): bone marrow derived stem cells in the treatment of age-related macular degeneration. Medicines. 2020;7:16. https://doi.org/10.3390/medicines7040016, 1–13.

Chapter 2
Tables

See Tables 2.1, 2.2 and 2.3.

At present there are 9 Stem Cell studies, 14 Gene Therapy studies, and 25 "Other" studies recruiting for AMD trials listed on clinicaltrials.gov. Of the 48 worldwide studies, 6 Stem Cell studies utilize a proprietary product (67%), 13 Gene Therapy studies utilize a proprietary product (93%), and 22 "Other" studies utilize a proprietary product (88%).

One study was U.S. National Eye Institute (NEI) supported (2%), 2 studies were patient funded (4%), and 12 studies were University/Hospital supported (25%). Sixty-nine percent of studies were corporate funded.

It is curious that in the United States, where millions of dollars in grants and donations are made for research, there was only 1 NEI-supported study, and no university/hospital-funded studies. Is the money being spent on research for other conditions, or is the work not being employed in a practical manner resulting in a clinical study?

J. N. Weiss, *Clinical Trials in Age-Related Macular Degeneration Treatment*,
https://doi.org/10.1007/978-3-031-58803-7_2

Table 2.1 Stem cell studies

	United States	Caribbean	China	Great Britain
Number of Studies	4	1	2	2
Non-Proprietary	1		2	
Proprietary	3	1		2
Support				
Corporate	2			
University/Hospital			2	2
NEI	1			
No Support	1	1		
Phase Not Applicable	1		1	1
Phase 1	1	1	1	1
Phase 1/2	2			
Phase 2				
Phase 2/3				
Phase 3				

Table 2.2 Gene studies

	United States	Canada	China
Number of Studies	7	1	6
Non-Proprietary			
Proprietary	7	1	5
Support			
Corporate	7		
University/Hospital			1
NEI			
No Support			
Phase Not Applicable			1
Phase 1	1		4
Phase 1/2	2	1	1
Phase 2	2		
Phase 2/3	1		
Phase 3	1		

Table 2.3 "Other treatments" studies

	United States	Australia	Austria	China	Italy	Korea	Norway	South America	Thailand
Number of Studies	10	2	2	6	1	1	1	1	1
Drug	8	1	1	6					1
Electrical	1					1			
Laser/Light		1			1		1	1	
Ultrasound	1								
Training			1						
Non-Proprietary	1	1			1				
Proprietary	9	1	2	6		1	1	1	1
Support									
Corporate	9	1		5		1		1	1
University/Hospital	1	1	2	1	1		1		
NEI									
No Support									
Phase Not Applicable	2	1	2		1	1	1	1	
Phase 1	2	1		1					
Phase 1/2									
Phase 2	5			1					1
Phase 2/3									
Phase 3	1			3					
Phase 4			1	1					

Chapter 3
Stem Cell Studies

United States

Recruiting

Safety and Tolerability of RPE Stem Cell-derived RPE (RPESC-RPE) Transplantation in Patients with Dry Age-Related Macular Degeneration (AMD)

ClinicalTrials.gov ID NCT04627428

Sponsor Luxa Biotechnology, LLC
Information provided by Luxa Biotechnology, LLC (Responsible Party)
Last Update Posted 2023-10-05

Study Overview

Brief Summary
The main objective of the study is evaluation of the safety and tolerability of RPESC-RPE-4W as therapy for dry AMD.

Detailed Description
RPESC-RPE-4W is Allogeneic RPE stem cell (RPESC)-derived RPE cells (RPESC-RPE) isolated from the RPE layer of human cadaveric eyes are transplanted under the macular.

This first-in-human Phase 1/2a open-label dose-escalation interventional study plans to enroll a total of 18 subjects.

Official Title
A Phase1/2a, Open-Label Study to Evaluate the Safety and Tolerability of RPE Stem Cell-Derived RPE (RPESC-RPE) Transplantation as Therapy for Dry Age-Related Macular Degeneration (AMD)

J. N. Weiss, *Clinical Trials in Age-Related Macular Degeneration Treatment*,
https://doi.org/10.1007/978-3-031-58803-7_3

Conditions
Dry Age-related Macular Degeneration

Intervention/Treatment
- Biological: RPESC-RPE-4W

Other Study ID Numbers
- RPESC-RPE-01
- U01EY030581 (U.S. NIH Grant/Contract)
- UG3EY031810 (U.S. NIH Grant/Contract)

Study Start (Actual)
2022-04-05

Primary Completion (Estimated)
2025-05-31

Study Completion (Estimated)
2025-05-31

Enrollment (Estimated)
18

Study Type
Interventional

Phase
Phase 1 Phase 2

Study Contact
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United States
Michigan Locations

Ann Arbor, Michigan, United States, 48105
Recruiting
University of Michigan Kellogg Eye Center

Contact
Rajesh C Rao, M.D.

Eligibility Criteria
Description

Inclusion Criteria
- Clinical diagnosis of dry AMD
- Ability to understand and give informed consent
- Adult male or female >55 years of age

- Medically suitable to undergo vitrectomy and subretinal injection (>60% on Karnofsky scale)
- Postmenopausal if the female (expected to be common for the age limitation), or the female partner of a male subject is unable to father children
- If the male is willing to use barrier and spermicidal contraception during the study

Exclusion Criteria
- Allergy or hypersensitivity to dilation drops or fluorescein
- Active major medical conditions limiting the ability to participate in the study
- Active malignancy or treatment with chemotherapy
- Systemic immunosuppressant therapy within the past six months
- History of toxoplasmosis, retinal histoplasmosis, or tuberculosis
- Receipt of investigational product (IP) in a clinical trial within the prior six months
- Any other medical condition, which, in the Investigator's judgment, will interfere with the subject's ability to comply with the protocol, compromises the subject safety, or interferes with the interpretation of the study results
- Pregnant or nursing females

Ages Eligible for Study
55 Years and older (Adult, Older Adult)

Sexes Eligible for Study
All

Accepts Healthy Volunteers
No

Primary Purpose: Treatment
Allocation: Non-Randomized
Interventional Model: Sequential Assignment
Masking: None (Open Label)

Arms and interventions

Participant group/arm	Intervention/treatment
Experimental: 50,000 cells Six patients will receive a single dose of 50,000 RPESC-RPE-4W cells in the eye	Biological: RPESC-RPE-4W • RPESC-RPE-4W
Experimental: 150,000 cells Six patients will receive a single dose of 150,000 RPESC-RPE-4W cells in the eye	Biological: RPESC-RPE-4W • RPESC-RPE-4W
Experimental: 250,000 cells Six patients will receive a single dose of 250,000 RPESC-RPE-4W cells in the eye	Biological: RPESC-RPE-4W • RPESC-RPE-4W

Primary outcome measures

Outcome measure	Measure description	Time frame
Safety and tolerability of RPESC-RPE-4W transplantation	The transplantation of RPESC-RPE-4W cells will be considered safe and tolerated in the absence of: • Decrease in visual acuity (VA) of more than 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (or to worse than counting fingers at three feet) from baseline • Any Grade 2 (CTCAE version 5) or greater adverse events (AE) related to the cell product and investigational interventions. • Any evidence that the cells are contaminated with an infectious agent or serious immune response to the cell product • Any evidence that the cells show tumorigenic potential	24 months

Secondary outcome measures

Outcome measure	Measure description	Time frame
Change in the mean of best-corrected visual acuity (BCVA)	Change in visual acuity will be measured by the ETDRS chart	24 months
Loss of ≥10 decibels of ten-degree average visual sensitivity microperimetry	Loss of ≥10 decibels of ten-degree average visual sensitivity will be measured by microperimetry	24 months
Change in GA lesion area	Change in GA lesion area will be measured	24 months
Evidence of structural changes	Structural evidence will be measured by OCT imaging, autofluorescence, fluorescein angiography, and fundus photography	24 months

Sponsor
Luxa Biotechnology, LLC

Collaborators
- National Institutes of Health (NIH)
- National Eye Institute (NEI)
- Regenerative Research Foundation

Investigators
- Principal Investigator: Rajesh C Rao, M.D., University of Michigan Kellogg Eye Center

General Publications
No publications available

United States

Recruiting

Autologous Transplantation of Induced Pluripotent Stem Cell-Derived Retinal Pigment Epithelium for Geographic Atrophy Associated with Age-Related Macular Degeneration

ClinicalTrials.gov ID NCT04339764

Sponsor National Eye Institute (NEI)
Information provided by the National Institutes of Health Clinical Center (CC) (National Eye Institute (NEI)) (Responsible Party)
Last Update Posted 2023-05-12

Study Overview

Brief Summary
Background
Age-related macular degeneration is a common eye disease in people over 50. The "dry" form of the disease can worsen into geographic atrophy, causing blind spots. Researchers want to learn if replacing older eye cells with younger ones can help treat this disease.

Objective
To test the safety of putting cells inside the eye as a possible future treatment for dry age-related macular degeneration.

Eligibility
People ages 55 and older who have geographic atrophy with loss of vision. People who have had "wet" macular degeneration in either eye are NOT eligible.

Design
Participants will be screened with:
- Medical history
- Physical exam
- Blood and urine tests
- Eye exam
- Eye photos
- Fluorescein angiography. An intravenous (IV) line is placed in an arm vein. A dye is injected. A camera takes pictures of the dye as it flows through the eyes' blood vessels.
- Electroretinography. An electrode is taped to the participant's forehead. They sit in the dark. After 30 min, numbing eye drops and contact lenses are placed in their eyes. They watch flashing lights.
- Tuberculosis test

- Chest X-ray
- Electrocardiography. Sticky pads are placed on participants' chests to record the heart's electrical activity.

Participants will have at least 14 study visits over 5 and a half years. They will repeat screening tests.

Participants will have retinal pigment epithelium (RPE) transplantation surgery in one eye. For this, cells from participants' blood are turned into RPE cells. These cells are placed in their eye through a cut in their retina. They will get dilating eye drops, an IV line, and anesthesia that may make them sleep. A gas bubble will be put in their eye to help it heal.

Participants will be contacted yearly for up to 15 years.

Detailed Description

Age-related macular degeneration (AMD) is a leading cause of vision loss among the elderly. There is no treatment for geographic atrophy (GA), the advanced stage of dry AMD, in which cells of the neurosensory retina and associated retinal pigment epithelium (RPE) gradually degenerate and die. Advances in stem cell biology allowing differentiation of pluripotent cells into RPE in vitro make feasible a cell-based strategy for the potential treatment of AMD, and recent methods for induced pluripotent stem cell (iPSC) the generation offer the promise of individualized autologous therapy. Such an approach involves the generation of iPSC from somatic cells taken from a patient with GA, differentiation of iPSC into RPE grown as a monolayer on a thin scaffold in vitro, and transplantation of the RPE/scaffold construct into a small region in the subretinal space of the same patient, with a goal of rescuing the overlying neurosensory retina from further degeneration.

Objective

To evaluate the safety and feasibility of subretinal transplantation of iPSC-derived RPE, grown as a monolayer on a biodegradable poly lactic-co-glycolic acid (PLGA) scaffold, as a potential autologous cell-based therapy for GA associated with AMD.

Study Population: Five participants will undergo RPE transplantation in one eye. Eligible eyes will have GA, best-corrected visual acuity (BCVA) between 20/100 and inclusive of counting fingers (CF), and a fellow eye that has the same or better BCVA. If the National Eye Institute (NEI) Data and Safety Monitoring Committee (DSMC) gives clearance to proceed based on a review of data from the first cohort, a second cohort of up to seven additional participants with GA, BCVA between 20/80 and CF (inclusive) in the eye being considered for RPE transplantation, and same or better visual acuity in the other eye may undergo the procedure to gather additional safety and potential efficacy data useful for planning future studies. Up to 20 participants may be enrolled to allow for screening failures, for participants withdrawing from the study prior to RPE transplantation, or cases where the RPE cell transplantation does not occur due to intraoperative surgical considerations.

Design
In this Phase I/IIa, prospective, single-arm, single-center clinical trial, participants will undergo subretinal transplantation of autologous iPSC-derived RPE in one eye and will be followed for five years after surgery.

Outcome Measures
The primary outcome measure is the safety of RPE/PLGA transplantation, as determined by the assessment of visual acuity change and summary of adverse events at 12 months after RPE/PLGA transplantation. Secondary outcome measures include visual acuity change and adverse event reporting at 24 and 60 months, and changes in the following at 12, 24, and 60 months as compared with baseline, assessed in the transplanted region, and compared where applicable with other areas in the macula, and/or with corresponding regions in the fellow eye: retinal sensitivity and fixation parameters assessed by microperimetry; multifocal electroretinography (mfERG) responses; macular structure on cross-sectional and en face imaging by optical coherence tomography (OCT); macular features on color, single-wavelength reflectance, and fundus autofluorescence (FAF) photography; and fluorescein angiography (FA). Some NEI participants may undergo imaging of photoreceptor/RPE features using adaptive-optics-assisted macular imaging under a separate protocol (e.g., 15-EI-0020).

Official Title
A Phase I/IIa Trial for Autologous Transplantation of Induced Pluripotent Stem Cell-Derived Retinal Pigment Epithelium for Geographic Atrophy Associated With Age-Related Macular Degeneration

Conditions
Age-Related Macular Degeneration

Intervention/Treatment
- Drug: iPSC-derived RPE/PLGA transplantation

Other Study ID Numbers
- 200052
- 20-EI-0052

Study Start (Actual)
2020-09-23

Primary Completion (Estimated)
2029-05-31

Study Completion (Estimated)
2029-05-31

Enrollment (Estimated)
20

Study Type
Interventional

Phase
Phase 1 Phase 2

Study Contact
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Study Contact Backup
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Maryland Locations

Bethesda, Maryland, United States, 20892
Recruiting
National Institutes of Health Clinical Center

Contact
For more information at the NIH Clinical Center contact the Office of Patient Recruitment (OPR)
800-411-1222 ext TTY8664111010 prpl@cc.nih.gov

Eligibility Criteria
Description

Inclusion Criteria
To be eligible, the following inclusion criteria must be met, where applicable.

- Participants must be 55 years of age or older
- Participants must have a diagnosis of AMD, defined as the presence (or history, as documented in available color fundus photographs) of at least one medium or large druse (greater than or equal to 63-micrometer diameter) in the macula in at least one eye; and the presence of GA in at least one eye.
- Participants must understand and sign the protocol informed consent document.
- Any participant of childbearing potential must have a negative pregnancy test at screening and must be willing to undergo pregnancy testing prior to RPE transplantation.
- Any participant of childbearing potential and any participant able to father children must have (or have a partner who has) had a hysterectomy or vasectomy, be completely abstinent from intercourse, or must agree to practice an effective method of contraception through Month 12 in the study. Acceptable methods of contraception include:
  - Hormonal contraception (i.e., birth control pills, injected hormones, dermal patch, or vaginal ring)
  - Intrauterine device
  - Barrier methods (diaphragm, condom) with spermicide or
  - Surgical sterilization (tubal ligation)

- Participants must be medically able to comply with the study treatment (including the ability to safely receive anesthesia for surgery), study testing and procedures, and follow-up visits.

Study Eye Inclusion Criteria

- The study eye must have one or more regions of geographic atrophy with a total area of 1 disc area or more. A region of geographic atrophy is defined as an area of uniform hypofluorescence on fundus autofluorescence (FAF) imaging, with greatest linear dimension at least 500 micrometers, with a border within 500 micrometers of the foveal center, not compatible with pigmentary changes, drusen, RPE detachment, drusenoid RPE detachment, hemorrhage, or another lesion. (Note: If macular geographic atrophy is contiguous with peripapillary atrophy, complicating the calculation of total area, only atrophy temporal to a vertical line placed a half-disc diameter temporal to the temporal border of the disc will be included in the total area of geographic atrophy calculated for eligibility purposes.)
- For participants in the first cohort, the study eye must have an ETDRS best-corrected visual acuity (BCVA) letter score of less than or equal to 53 and greater than or equal to CF (i.e., Snellen equivalent between 20/100 and CF), and the fellow eye must have a letter score no more than five letters worse than the study eye using Electronic Visual Acuity (EVA) testing. (Note: Letter scores within five or fewer letters of each other are accordingly considered equal for eligibility determination, and other factors may be used to select the study eye if both are eligible by BCVA.)
- For participants in the second cohort, the study eye must have an ETDRS best-corrected visual acuity (BCVA) letter score of less than or equal to 58 and greater than or equal to CF (i.e., Snellen equivalent between 20/80 and CF), and the fellow eye must have a letter score no more than five letters worse than the study eye using Electronic Visual Acuity (EVA) testing. (Note: Letter scores within five or fewer letters of each other are accordingly considered equal for eligibility determination, and other factors may be used to select the study eye if both are eligible by BCVA.)
- The compromise in visual acuity for the study eye must be judged predominantly secondary to dry AMD, in the judgment of the investigator.
- The study eye must have clarity of ocular media and a degree of pupil dilation sufficient to permit adequate fundus photography and safe vitrectomy surgery.
- The study eye must be either pseudophakic or aphakic.

Exclusion Criteria

A participant is not eligible if any of the following exclusion criteria are present:

- Participant is actively receiving another study medication/investigational product (IP).
- Participant has any condition that significantly increases the risk of systemic corticosteroids or systemic steroid-sparing immuno-modulatory agents, such as uncontrolled diabetes mellitus, chronic hepatitis or liver failure, chronic renal failure, or present infection with HIV, syphilis, tuberculosis, hepatitis B, or hepa-

titis C (past infection now resolved, where applicable, is not exclusionary; but persistent infection, even if latent, is exclusionary).
- Participant has a diagnosis of a malignancy expected to affect two-year survival.
- Participant is pregnant, breastfeeding, or planning to become pregnant through the first 12 months of the study.
- Participant has a family history of a retinal degeneration other than AMD suspected to play a role in the ocular phenotype of the participant in the judgment of the investigator, based on disease features and mode of inheritance, such as in a case of autosomal dominant retinal degeneration in a parent or child.
- Participant is taking, or has taken within the previous year, medication with known potential toxicity to the retina, optic nerve, or lens (such as chloroquine, hydroxychloroquine, and ethambutol).
- Participant is unable or unwilling to give informed consent that includes the use of medical records and clinical samples for current and future research.

Study/Eye Exclusion Criteria
- The study eye must not have macular subretinal or choroidal neovascularization, as assessed by FA and OCT; or any history of such neovascularization (as assessed by past available records or images).
- The study eye must not have any serous or hemorrhagic pigment epithelial detachment, as assessed by FA and OCT.
- The study eye must not have any history of photodynamic therapy (PDT) or macular thermal laser photocoagulation, or history of intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents or corticosteroids (excepting medications used peri-operatively at prior cataract surgery).
- The study eye must not have an axial length > 25.0 mm.
- The study eye must not have had any surgery in the previous 12 weeks, or laser capsulotomy in the previous four weeks.
- The study eye must not have chronic glaucoma; or significant ocular hypertension, defined as documented intraocular pressure of greater than or equal to 26 mmHg on at least two occasions in the absence of self-limited acute glaucoma; or a history of probable or definite steroid response manifesting as acute glaucoma or ocular hypertension, even if self-limited and no longer present; and the fellow eye must not have evidence for present or past glaucoma or ocular hypertension judged to significantly impact the risk of glaucoma in the study eye (including history of probable or definite steroid response). (Note: History of self-limited acute glaucoma in a study or fellow eye, if not secondary to steroid response, and if now resolved and not expected to recur (e.g., history of elevated intraocular pressure from retained visco-elastic after cataract surgery), is not exclusionary. History of glaucoma or ocular hypertension in the fellow eye, if not felt to significantly impact the risk of glaucoma in the study eye, is not exclusionary.)
- The study eye must not have a condition materially increasing the risks of surgery or potentially affecting visual function over the next two years in the judgment of the investigator, such as chronic uveitis, diabetic retinopathy, ker-

atitis, scleritis, optic neuropathy, untreated retinal detachment, macular edema from prior vein occlusion or other cause, proliferative vitreoretinopathy (PVR), vitreous hemorrhage, and pathologic myopia. A history of such conditions is not exclusionary, if judged to not materially increase risks of surgery or to potentially affect vision in the next two years in the opinion of the investigator.

Ages Eligible for Study
55 Years and older (Adult, Older Adult)

Sexes Eligible for Study
All

Accepts Healthy Volunteers
No
Study Plan

Design Details
Primary Purpose: Treatment
Allocation: N/A
Interventional Model: Single Group Assignment
Masking: None (Open Label)

Arms and interventions

Participant group/arm	Intervention/treatment
Experimental: Participants receiving intervention Participants receiving intervention	Drug: iPSC-derived RPE/PLGA transplantation • iPSC-derived RPE/PLGA transplantation

Primary outcome measures

Outcome measure	Measure description	Time frame
Visual acuity change	Safety measure	12, 24, and 60 month
Summary of adverse events	Safety measure	12, 24, and 60 month

Secondary outcome measures

Outcome measure	Measure description	Time frame
Retinal Structure (optical coherence tomography)	Safety and efficacy measure	12, 24, and 60 month
Retinal sensitivity and fixation (microperimetry)	Safety and efficacy measure	12, 24, and 60 month
Multifocal electroretinography responses	Safety and efficacy measure	12, 24, and 60 month
Retinal Structure (color and autofluorescence imaging)	Safety and efficacy measure	12, 24, and 60 month
Retinal structure (fluorescein angiography)	Safety and efficacy measure	12, 24, and 60 month

Sponsor
National Eye Institute (NEI)

Collaborators
No information provided

Investigators
- Principal Investigator: M. Teresa Magone de Quadros Costa, M.D., National Eye Institute (NEI)

General Publications
No publications available

United States

Recruiting

Stem Cell Ophthalmology Treatment Study II (SCOTS2)

ClinicalTrials.gov ID NCT03011541

Sponsor MD Stem Cells
Information provided by MD Stem Cells (Responsible Party)
Last Update Posted 2023-06-06

Study Overview

Brief Summary
This study will evaluate the use of autologous bone marrow derived stem cells (BMSC) for the treatment of retinal and optic nerve damage or disease.

Detailed Description
Eyes with the loss of vision from retinal or optic nerve conditions generally considered irreversible will be treated with a combination of injections of autologous bone marrow derived stem cells isolated from the bone marrow using standard medical and surgical practices. Retinal conditions may include degenerative, ischemic, or physical damage (examples may include macular degeneration, hereditary retinal dystrophies such as retinitis pigmentosa, Stargardt, non-perfusion retinopathies, and post retinal detachment). Optic Nerve conditions may include degenerative, ischemic, or physical damage (examples may include optic nerve damage from glaucoma, compression, ischemic optic neuropathy, optic atrophy). Injections may include retrobulbar, subtenon, intravitreal, intraocular, subretinal, and intravenous. Patients will be followed for 12 months with serial comprehensive eye examinations including relevant imaging and diagnostic ophthalmic testing.

Official Title
Bone Marrow Derived Stem Cell Ophthalmology Treatment Study II

Conditions
Retinal Disease
Age-Related Macular Degeneration
Retinitis Pigmentosa
Stargardt Disease
Optic Neuropathy
Nonarteritic Ischemic Optic Neuropathy
Optic Atrophy
Optic Nerve Disease
Glaucoma
Leber Hereditary Optic Neuropathy
Blindness
Vision Loss Night
Vision Loss Partial
Vision, Low
Retinopathy
Maculopathy
Macular Degeneration
Retina Atrophy

Intervention/Treatment
- Procedure: Arm 1

Other Study ID Numbers
- SCOTS2

Study Start (Actual)
2016-01

Primary Completion (Estimated)
2024-07

Study Completion (Estimated)
2025-07

Enrollment (Estimated)
500

Study Type
Interventional

Phase
Not Applicable

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Recruiting
Medcare Orthopaedics & Spine Hospital

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Eligibility Criteria
Description

Inclusion Criteria
- Have objective, documented damage to the retina or optic nerve unlikely to improve or
- Have objective, documented damage to the retina or optic nerve that is progressive and has less than or equal to 20/30 best-corrected central visual acuity in one or both eyes and/or an abnormal visual field in one or both eyes.
- Be at least 3 months post-surgical treatment intended to treat any ophthalmologic disease and stable.

- If under current medical therapy (pharmacologic treatment) for a retinal or optic nerve disease be considered stable on that treatment and unlikely to have visual function improvement (e.g., glaucoma with intraocular pressure stable on topical medications but visual field damage).
- Have the potential for improvement with BMSC treatment and be at minimal risk of any potential harm from the procedure.
- Be over the age of 18.
- Be medically stable and able to be medically cleared by their primary care physician or a licensed primary care practitioner for the procedure.
- Medical clearance means that in the estimation of the primary care practitioner, the patient can reasonably be expected to undergo the procedure without significant medical risk to health.

Exclusion Criteria
- Patients who are not capable of an adequate ophthalmologic examination or evaluation to document the pathology.
- Patients who are not capable or not willing to undergo follow-up eye exams with the Principal Investigator or their ophthalmologist or optometrist as outlined in the protocol.
- Patients who are not capable of providing informed consent.
- Patients who may be at significant risk to general health or to the eyes and visual function should they undergo the procedure.

Ages Eligible for Study
18 Years and older (Adult, Older Adult)

Sexes Eligible for Study
All

Accepts Healthy Volunteers
No

Design Details
Primary Purpose: Treatment
Allocation: N/A
Interventional Model: Single Group Assignment
Interventional Model Description: Single Arm—Arm 1. Comparator is the natural history of the disease
Masking: None (Open Label)