Macular Degeneration Foundation®

Our focus is your vision

Research update 2009

Macular Degeneration Research

Researchers across the world are working on Macular Degeneration to find reasons for this disease and the answers needed. There are many ongoing clinical trials and the Foundation is proud of the many brilliant and dedicated Australian researchers who form part of this international team. The following is a summary of research occurring around the world.

Genetics

Approximately 15 genes have been linked with MD and the strongest associated genes are complement factor H and ARMS 2. Complement factor H has been linked with increased risk of MD progression, as well as a larger (choroidal neovascular) lesion size for those with wet MD.

New targets for MD therapy are being identified, guided by genetic research. Current best practice for wet MD relies on the suppression of neovascularisation but does not address the underlying disease or its progression. Therapies in the future might not only prevent the progression of neovascularisation, but may also lead to effective prevention at earlier stages which could delay the onset of MD.

Devices

Intraocular Implant

The intraocular implant consists of human cells that have been genetically modified to secrete ciliary neurotrophic factor (CNTF). CNTF is a growth factor capable of rescuing dying photoreceptors and protecting them from cell death. CNTF is delivered directly to the back of the eye by an Encapsulated Cell Technology (ECT) device which is implanted during a short outpatient procedure.

The Phase II trial results have indicated that the device slowed the loss of vision in subjects with dry MD. There were no associated serious adverse effects reported and both the device and the procedure were well-tolerated.

Implantable Miniature Telescope (IMT)

The implantable miniature telescope (IMT) is geared towards patients with advanced MD in both eyes resulting in severe vision loss. With the IMT, the image is enlarged so that it is projected onto healthy areas of the retina enabling the majority of the image to be seen. Unlike an external telescope, scanning is done with the eye rather than head movement.

The IMT device now meets all of the US Food and Drug Administration (FDA) requirements for safety and efficacy. In March 2009 the FDA panel gave unanimous recommendation for approval. Full approval is pending.

Retinal Prosthetic Devices

A long-term clinical trial is underway in the US and Europe of a retinal prosthesis that provides sight to patients blinded from retinal degenerations, such as retinitis pigmentosa and potentially end-stage MD. The device consists of a tiny camera

and transmitter mounted in eyeglasses which converts the image to an electronic signal. Patients learn to interpret the visual patterns and produce them into meaningful images. While progress in the field is interesting, potential commercialisation of these devices is still a number of years away.

Treatment

VEGF Trap-Eye

The VEGF Trap is an injection into the eye that is designed to bind all forms of Vascular Endothelial Growth Factor-A (VEGF-A) and Placental Growth Factor (PLGF). Both VEGF-A and PLGF are proteins involved in the abnormal growth of new blood vessels.

This injection offers the potential for increased efficacy or decreased treatment duration. Based on the positive results achieved in studies, two pivotal studies are now fully enrolled in the US with 1,200 patients called VIEW 1 and VIEW 2. The VEGF Trap-Eye is being evaluated using four and eight week dosing intervals.

Radiation for Wet MD

Radiation is gaining attention again as a potential treatment for wet MD. Unlike anti-VEGF agents, radiation is thought to eliminate CNV vessels permanently, rather than simply suppressing them.

Preliminary studies from the MERITAGE 1 study using epimacular brachytherapy suggest that visual acuity can be improved in a majority of patients by inserting a device into the eye to deliver targeted radiation. More information is forthcoming from two large Phase III studies (CABERNET and MERITAGE II).

A Phase I trial in Mexico City is evaluating the safety, efficacy and biological effect of the IRAY in MD patients. The IRAY is an office-based surgery where the physician delivers low dose, low energy, x-ray radiation to the macula. This is performed in a 10 to 20 minute procedure (in conjunction with an initial anti-VEGF dose). IRAY will enter pivotal studies in Europe and the US within the next 18 months.

Eye Drops

Eye drops could offer patients with wet MD an easy to administer alternative to frequent injections. Eye drops could also offer significant cost, patient compliance and convenience advantages.

Pazopanib is currently being investiged for use by patients with wet MD. Pazopanib is a second-generation multi-targeted tyrosine kinase inhibitor. In the case of VEGF, a kinase inhibitor can prevent blood vessels from growing and leaking. Change in visual acuity was statistically significantly improved in the high dose group. Plans are underway for a larger Phase IIb study to further investigate these observations.

Anti-VEGF Injections and PDT

Lucentis is the current standard for managing neovascular MD. There are currently very few combined treatments used in practice, however there is very good rationale for combining anti-VEGF with a number of different therapies. The goal is for clinicians to improve visual results and decrease the number of injections.

Good safety and efficacy data to combine verteporfin PDT and Lucentis were observed

in FOCUS and PROTECT trials. A large set of clinical trials (SUMMIT) are now underway to validate and expand on these findings.

Clinical Trials for Avastin vs Lucentis

Trials are comparing Lucentis and Avastin in the US (CATT), UK (IVAN) Germany (VIBERA), Austria (MANTA), Norway (LUCAS) and France (GEFAL). The largest trials are in the US and UK.

In the US the CATT study has enrolled more than 1,130 patients in the multi-centered trial to assess the relative safety and efficacy of Lucentis and Avastin. CATT is funded by the National Eye Institute (NEI). In early 2011, CATT is expected to report results on the head-to-head trials for Lucentis and Avastin. Other studies will report in 2011 and 2012.

Dry MD

Dry MD is a human disease without any animal correlates. Clues to treating dry MD will be gathered from human clinical trials. Results of major trials within the next several years cover three strategies which have emerged in major areas of therapeutic areas of investigation: Preservation of photoreceptors and RPE (neuroprotection); Prevention of oxidative damage; and Suppression of inflammation.

There are a number of Phase I and Phase II clinical trials ongoing in the area of preserving photoreceptors and RPE. A Phase III trial is currently testing a drug called trimetazidine (Vastarel) to improve choroidal circulation in patients with dry MD and slow down the conversion of dry MD to wet MD.

Oxidative stress is considered to be a driving force in disease progression. In addition to the AREDS II trial (Phase III) a topical antioxidant (OT-551) eye drop is being evaluated as a treatment for dry MD and is currently in Phase II (OMEGA) trials.

There are more than ten pre-clinical, Phase I and II clinical trials in the area of research to suppress inflammation.

Laser for Dry MD

Researchers at the Centre for Eye Research Australia will begin a trial using laser therapy aimed at stopping the progression of dry MD. The laser therapy involves a specially designed novel laser device that delivers a controlled nanosecond dose of laser energy into the eye.

The laser will be used in the early stages of MD and it is hoped that it will eliminate drusen and halt or partially reverse the progression of MD before it advances.

Nutrition

It is well established that patients with moderate to advanced MD take the current recommended AREDS formula (zinc, vitamins C, E, and beta carotene)[1]. The AREDS II trial is now underway to determine the 'next generation' of supplementation. It is sponsored by the US National Eye Institute, the objective being to evaluate the effect of lutein/zeaxanthin and/or omega-3 on the progression of MD to advanced stages. Enrolment is complete with more than 4,000 patients and results are expected in 2010.

Lutein and zeaxanthin are dietary factors specially concentrated in the macula. Recent studies indicate that daily supplement of lutein and zeaxanthin with at least 6 mgs may be beneficial.

A study conducted by the US National Eye Institute has suggested that daily supplementation of folic acid and vitamins B6 and B12 may reduce the risk of developing early stages of MD.

Cataract Surgery

While cataract surgery can improve visual function and quality of life of patients with MD, there have been a number of concerns about cataract surgery accelerating the development or progression of MD.

Recent reports evaluating the original AREDS study data have concluded there was no clinically important increase in risk that cataract surgeries accelerate the development of MD. It may be that MD was pre-existing, but undetectable or undetected. People with varying levels of MD can have vision and quality of life improvements with cataract surgery.

Stem Cell

Stem Cell research is looking to commence in the US and UK in the next few years.

UK: The London Project to Cure Blindness

The London Project to Cure Blindness is a five year research project at the University College London and Moorfields Eye Hospital in the UK which aims to develop a surgical cell therapy for MD. This therapy aims to restore sight to people with MD.

The trials will use human embryonic stem cells (hES) that have been transformed into retinal epithelium cells (RPE) to replace the cells at the back of the eye.

Clinical trials should commence by 2011. However since this is the first human embryonic stem cell trial in humans in the UK, the clinical trial will depend on the regulatory pathway.

US: Stargardt's Macular Dystrophy Stem Cell Trial

Researchers in the US have applied to the US Food and Drug Administration for approval to test retinal cells grown from stem cells in people with Stargardt's macular dystrophy. The disease is a childhood version of MD.

In the trial new RPE cells will be derived from hES cells. The RPE cells have been shown to improve vision in animals, with one study restoring eye function in rats and mice to 'near-normal' levels. Another study boosted rats' vision to 70% that of healthy animals. No adverse side effects were found in any of the company's pre-clinical studies.

The clinical trial could begin early next year and if results are promising permission will be sought to use this therapy to treat MD.

Please Note:

1. Beta carotene has been removed in some Australian products due to the increased risk of lung cancer in smokers. The Foundation supports the removal of beta carotene in such product).
2. This report is about ongoing research. Any consideration of treatment or management should always be discussed with your specialist.
3. The Foundation recognises and respects different points of view concerning stem cell research. Our role is to simply report on all research occurring for your information.
4. MDF acknowledges and thanks the AMD Alliance International for information on research.