MacularNEWS

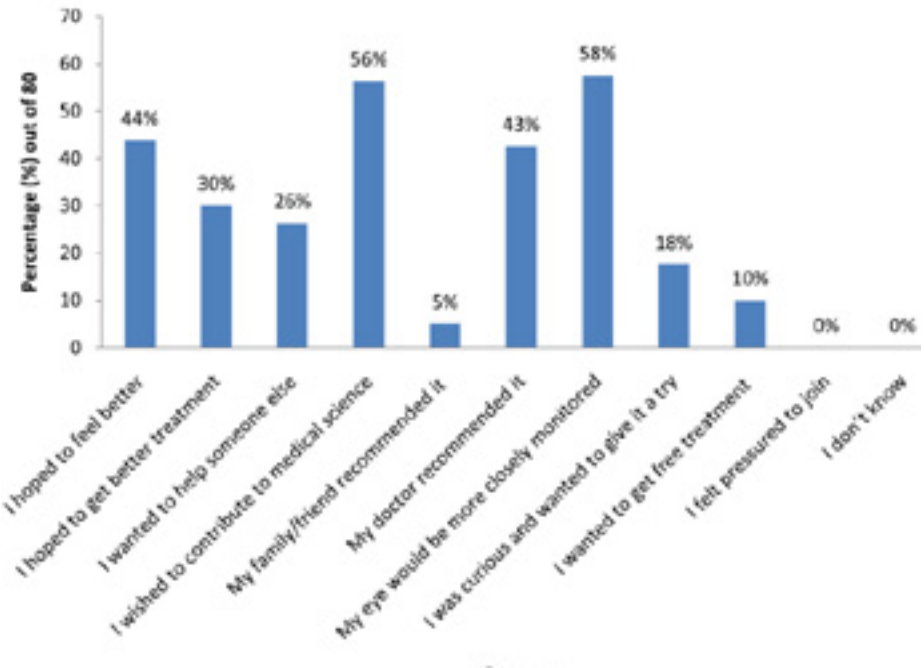
The Clinical Research Unit (CRU) of the Macula Research Group (MRG) is an internationally certified clinical trial unit that conducts randomised clinical trials in macula and retinal disease.

Patients enrolled in our clinical trials undergo assessments and are offered emerging treatments which are provided free of charge and may not be available for a number of years for ordinary patients in Australia.

Why Clinical Trials?

Clinical trials are crucial in the development of new treatments, and the safety monitoring and evaluation of the effectiveness of existing treatments. To ensure that we are providing quality patient care, our team conducted a study (Au et al., 2015) evaluating our patients' experience of participating in clinical trials of new treatments for macular disease. Most patients reported a positive experience: **94 percent** said they would recommend participation to others and **78 percent** said they would consider participating in another trial. The main causes of dissatisfaction related to waiting times and transport acccessibility. Nevertheless, the potential benefits of participating in a clinical trial seemed to outweigh the inconveniences (Fig.1).

1 *Figure 1:* Patient reasons for joining the trial at Sydney Eye Hospital (n=246)



In this edition, I am pleased to share our research into treatment outcomes for patients with Diabetic Macular Oedema (DMO) and interviews with some of our clinical research staff and patients.

Our research relies exclusively on external grants and fundraising.

If you are in a position to support macular research, please know that we are extremely grateful and that your donation will be well used.

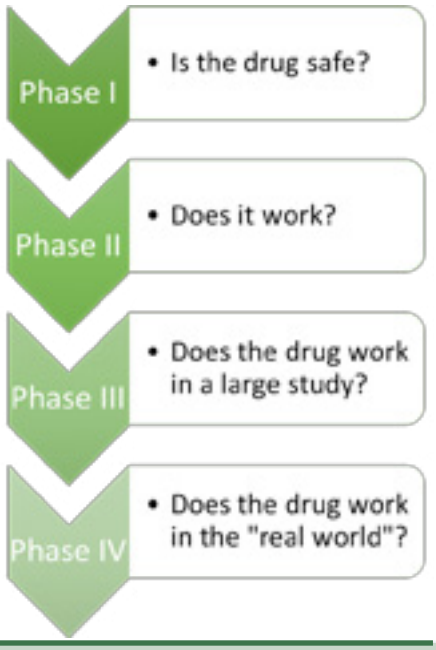
You may also like to consider remembering macular research in your will.

Thank you for your support.

Prof. Mark Gillies
Macula Research Group

To stay updated on all macular research and patient events please email macular.news@sydney.edu.au and ask to be placed on our e-mail notification list.

Trial to Treatment: Stages of Clinical Trials



It is estimated that it takes anywhere between 10 to 15 years for a new drug to go through the process of clinical trials in order to be safely approved for use on patients. Typically, clinical trials can be categorised into four different phases:

Phase I: Initial phase to determine whether the drug is safe and the dose tolerable.

Phase II: The first indication of whether the drug works.

Phase III: The formal testing of a drug in larger studies, based on the results of Phase II studies, which are required for the drug to be registered for use.

Phase IV: "Observational" studies to test whether drugs that passed Phase III trials are effective when used in "real world" clinical practice.

Our Success Stories

One of the CRU's most influential recent studies was a direct head-to-head comparison of two drugs that are used to treat diabetic macular oedema (DMO), the most common cause of loss of vision in people with diabetes. We provided the first evidence that injections of steroids into the eye were effective for this condition over 10 years ago. The other class of drug that is used for DMO, vascular endothelial growth factor inhibitors, were first used for neovascular ("wet") age-related macular degeneration but they are also effective for DMO. Steroids tend to be stronger and last longer, but they have more side effects, particularly the formation of cataract and elevated intraocular pressure. We found similar improvements in vision for the steroid we tested, a slow release formulation of dexamethasone (Ozurdex), and the VEGF inhibitor bevacizumab (Avastin). This study supported the use of the dexamthasone implant in eyes with DMO, especially if they have already had their cataract removed. The steroid was only required on average five times over two years compared with 13 injections of the VEGF inhibitor. It also supports the use of steroids when the response to VEGF inhibitors is sub-optimal.

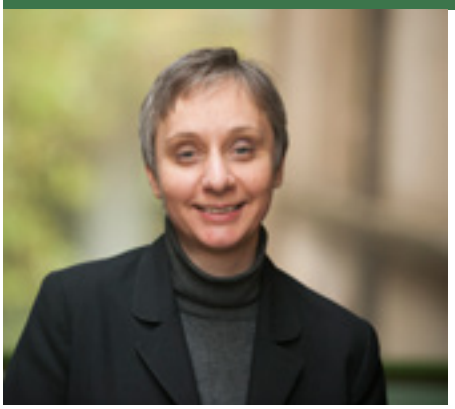
Sponsored versus Investigator Initiated Trials

The MRG participate in sponsored trials and conduct important investigator initiated trials. Sponsored studies are funded by (for example) pharmaceutical companies. The benefit of being involved in these trials is that we can offer patients the opportunity of having access to emerging treatments, which gives our ophthalmologists experience in the new treatments before they become widely available. We are currently involved in sponsored trials in wet macular degeneration, a dry form of macular degeneration called geographic atrophy, macular telangiectasia type II and retinal vein occlusion (commencing shortly).

Investigator initiated trials are studies which are designed by our own ophthalmologists. These are trials which are answering important questions about macular diseases, which may not necessarily have a commercial benefit, though may have a significant impact on the way macular diseases are treated and improve outcomes for patients with macular disease. These trials are supported in part, or solely, by generous donations or grant funding.

Our two major investigator initiated studies currently underway are in diabetic macular oedema. One trial is looking to see whether combining a standard laser treatment along with the approved vascular endothelial growth factor inhibitor injection aflibercept (Eylea), is better than Eylea injections on their own. Our other trial, described in our Autumn 2016 Newsletter, is investigating the use of a new near infrared light in the treatment of this condition.

Working in Clinical Trials - Meet our team



Maria Williams
Clinical Research Manager of the Macular Research Group (MRG)

Maria Williams came to the Save Sight Institute 14 years ago, having previously worked in Endocrinology and Oncology (cancer) clinical research. Maria initially worked as a study coordinator including seeing patients in the research clinic. As the research group grew, she moved into a management and supervisory role and other talented staff have taken over the day to day research visits in the clinic. Maria shares her insight on running the MRG Clinical Research Unit.

Complexity of Trials

I noticed immediately that ophthalmology trials are far more complicated than oncology trials, mainly due to the multiple teams required to run the trials, and that all testing is performed by the research staff and not outsourced to other providers.

Masked and Unmasked Teams

Many trials require a masked team (the team that does not know the treatment allocation of each patient) and an unmasked team (the team that does know the treatment allocation of each patient). Having separate teams involved in certain aspects of the trial aids in reducing bias.

The unmasked team is not allowed to reveal the treatment allocation to the masked team. There are usually three different roles within the unmasked team: the doctor performing the procedure, the assistant helping the doctor during the procedure and the pharmacy department, which dispenses the drug.

The masked team is also segregated into the assessing doctor, the orthoptist doing the imaging (scanning and photography of the eye), the orthoptist performing the vision testing, the coordinator and the laboratory technician processing the pathology samples. Some trials do not allow overlapping of these roles within the masked team.

To further complicate matters we also need a backup person for each role in the trial, so each person must have at least one other person who can perform the same role in case of holidays, sick leave or other emergencies. However, the backup person is not allowed to overlap with the other roles. This all means that some trials need as many as 16 available staff just to process one single patient visit!

The Rewards - Our Patients

The nicest part of working in clinical trials is working with the patients. Since the patients are often with the research group for an extended time, we get to know them well and they also get to know the research staff. It can be quite sad when we have to say goodbye to our research patients at the end of the trial.

We are extremely grateful to our patients who have considered participating in a trial. Being in a clinical trial is not for everyone.

The Results

It is enormously rewarding to be involved in developing new ground breaking treatments. Our unit has been involved in trials that have now produced the new standard of care treatments for conditions such as wet macular degeneration, diabetic macular oedema and retinal vein occlusion.

"Every data point, every image and every drop of blood we collect during the trials are precious. When combined together and analysed, this data may hold the key to the next new treatment for macula disease."

Professor Mark Gillies with attendees at an information session about macular degeneration.

Antoinette De Zoysa
Clinical Research Orthoptist

I have been a part of the MRG team for the past 2 months and it has been an *eye*-opening experience working in the field of research and clinical trials.

The way in which our team is involved in not only site-specific research projects but also being a part of global clinical trials is something I have found to be particularly interesting and fascinating.

As I have a background working as a clinical orthoptist in the private and public sector, I can appreciate how these new and upcoming treatments will one day benefit patients. It makes all the hard work we do here at the Institute worthwhile.

PATIENT EXPERIENCE: MEET KAREN

Clinical Trial Patient

I have nothing but praise for the entire Macula Research Group who have looked after me for a period of time now (10 years!).

The staff involved with the MRG are very friendly and accommodating. They are always willing to answer any questions that I have and go out of their way to assist me with fitting in my scheduled visits around my personal and work commitments.

"During my visits, all the staff are welcoming and make me feel like I am contributing to their great work - they are true professionals."

Haipha Ali
Clinical Research Orthoptist

I have worked in clinical trials as a Research Orthoptist for over 10 years and my experience has been a very positive one! My role has varied from coordinating to assessing vision, as well as various imaging techniques. The highlights in working in clinical research definitely have to be the patient contact. Having that interaction on a regular basis allows us to develop a bond with the patients and see the resilience of the human spirit! And, of course, other highlights have to be the treatments that improve the patient's vision and have such an impact on their lives.

Please do not hesitate to contact us if you, or someone you know, are interested in joining a clinical trial for macular disease. For more information on the study, the journal article can be accessed for free online.

Reference:
Au, C., Fardell, N., Williams, M., Fraser-Bell, S., Campain, A. and Gillies, M. (2015). Patient experiences in retinal trials: a cross-sectional study. BMC Ophthalmology, 15(1).

If you would like to make a tax-deductible donation or discuss leaving a bequest to support macular research please visit our website, call us on (02) 9382 7309 or post a cheque to Save Sight Institute, South Block, Sydney Eye Hospital,
8 Macquarie Street Sydney NSW 2000.

Save Sight Institute is a Centre of The University of Sydney.

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