

MacularNEWS

Spring 2023 : Edition 27

INSITE-DME study for diabetic macular oedema

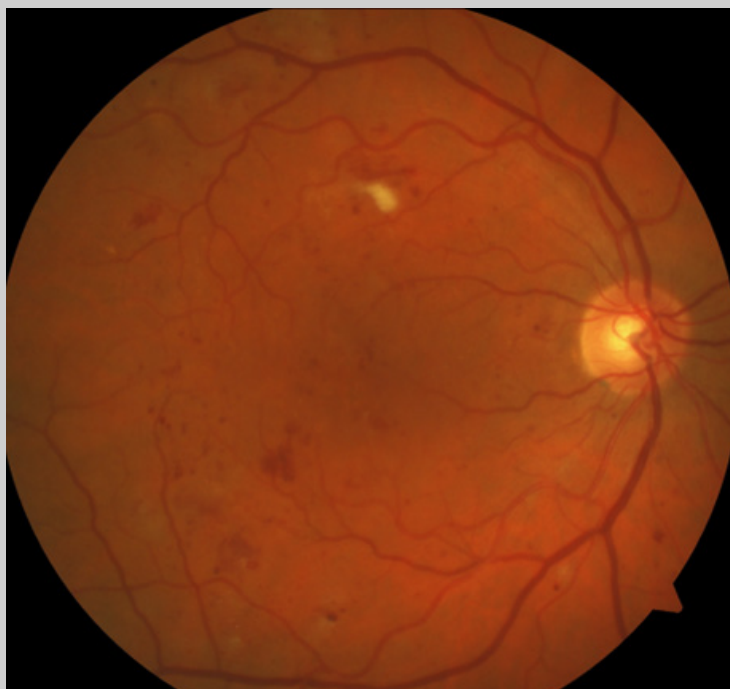


Figure 1: Colour fundus photo of a right eye showing features of diabetic retinopathy

Approximately 1.5 million Australians have been diagnosed with diabetes and a further half a million are likely to have diabetes but remain undiagnosed.¹ The number of people with diabetes worldwide is set to rise with an estimated increase by 69% in the developing world and 20% in the developed world by 2030.² Similar trends are expected in Australia.

In Australia, 300,000–400,000 people have diabetic retinopathy³ and 87,400 of those have diabetic macular oedema (DMO).⁴ High levels of blood glucose due to diabetes cause changes in retinal vessels which then leak fluid. The fluid tends to settle centrally in the macula (macula oedema) affecting vision. DMO is a leading cause of vision loss in working aged Australians.



Director's Message

It's well-established that anti-VEGF injections reduce diabetic macula oedema, a leading cause of vision loss in working aged Australians. However, injections can be burdensome for both patients and our healthcare system, signalling the need for treatments that last longer between injections.

This issue of **MacularNEWS** looks at the INSITE-DME study, which will investigate the use of a new anti-VEGF injection in routine clinical practice. I hope you enjoy reading about the study.

A handwritten signature in black ink, appearing to read 'Mark Gillies'.

Professor Mark Gillies
Macula Research Group

MacularNEWS is now available digitally!
To subscribe, visit <http://tinyurl.com/macularnews>

The Macula Research Group has been involved in multiple investigator-initiated and pharmaceutical sponsored clinical trials improving visual outcomes of patients with DMO⁵⁻⁸. Eyes with DMO have increased amounts of a molecule called vascular endothelial derived growth factor (VEGF). There is robust evidence that reducing VEGF with anti-VEGF injections into the eye reduces DMO and improves vision such that it has become the gold standard treatment. However, it needs to be injected regularly leading to a significant burden on patients and health care systems. This has led to the desire for the development of treatments that could be given less often.

One way to reduce frequency of treatment is to block more than one pathway. Faricimab is a medication injected into the eye that inhibits both VEGF and another molecule Ang-2. This is thought to lead to longer duration of effect than drugs inhibiting VEGF alone. We had several patients from Sydney Eye Hospital in the RHINE study which investigated the use of Faricimab for DMO. Eyes with DMO that received Faricimab generally needed fewer injections than eyes that received Aflibercept⁹, a drug that has been available in Australia for more than 10 years. Due to the positive results from the RHINE study, Faricimab is now licensed in Australia and provided by the government for DMO in routine clinical practice. However, there can be a big difference between clinical trials and what happens when you see a doctor. We need more flexible ways to treat DMO that are more likely to work for patients and doctors.

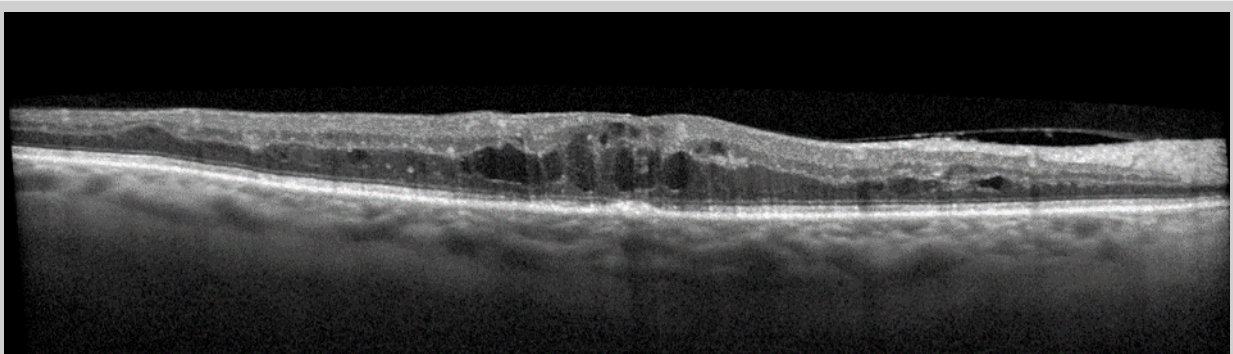


Figure 2: Optical coherence tomography (OCT) image through the right macula showing diabetic macular oedema as shown by the black cystic spaces within the retinal scan.

To address this, Associate Professor Samantha Fraser-Bell from the Macula Research Group has teamed up with investigators around the world, including Professor Varun Chaudhary from McMaster's university in Canada. Together they have designed an investigator-initiated study, called INSITE-DME comparing the vision gained when using fixed dosing of Faricimab (where Faricimab is given every eight weeks) compared to a treat and extend regimen (where the interval between injections is cautiously increased up to 24 weeks). These are simpler regimens than those used in the RHINE study and hence more likely to be used in routine clinical practice.

Other analyses will be performed including change vision related quality of life, change in diabetic retinopathy status and change in perfusion (blood supply) of the retina. It is important to have investigator-initiated studies that can assess new medications once they are approved to assess their effectiveness without the influence of the pharmaceutical companies which brought them to market. This international collaboration brings together people of specific skill sets but will also help to generalise the results to everyday patients. The study has started enrolling patients overseas and in Australia and we will share the results once we have them.

References

1. Diabetes Australia. Facts about diabetes in Australia. <https://www.diabetesaustralia.com.au/about-diabetes/diabetes-in-australia/>
2. Shaw J, Sicree R, Zimmet P, . Global Estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Clin Res Pract.* 2010;87(1):4-14.
3. Keel S, Xie, J, Foreman, J, van Wijnagaarden, Taylor, H, Drani, M. The Prevalence of Diabetic Retinopathy in Australian Adults with Self-Reported Diabetes: The National Eye Health Survey. *Ophthalmology.* 2017;125(2)doi:10.1016/j.ophtha.2017.02.004.
4. Deloitte Access Economics, Bayer Australia Ltd. The economic impact of diabetic macular oedema in Australia. 2015.
5. Gillies MC, Simpson JM, Gaston C, Hunt G, Ali H, Zhu M, Sutter F. Five-year results of a randomized trial with open-label extension of triamcinolone acetonide for refractory diabetic macular edema. *Ophthalmology.* 2009 Nov;116(11):2182-7
6. Fraser-Bell S, Lim LL, Campain A, Mehta H, Aroney C, Bryant J, Li J, Quin GJ, McAllister IL, Gillies MC. Bevacizumab or Dexamethasone Implants for DME: 2-year Results (The BEVORDEX Study). *Ophthalmology.* 2016 Jun;123(6):1399-401.
7. Shen W, Teo KYC, Wood JPM, Vaze A, Chidlow G, Ao J, Lee SR, Yam MX, Cornish EE, Fraser-Bell S, Casson RJ, Gillies MC. Preclinical and clinical studies of photobiomodulation therapy for macular oedema. *Diabetologia.* 2020 Sep;63(9):1900-1915.
8. Cornish EE, Wickremasinghe S, Mehta H, Lim L, Sandhu SS, Nguyen V, Gillies MC, Fraser-Bell S. Aflibercept monotherapy versus aflibercept with targeted retinal laser to peripheral retinal ischemia for diabetic macular oedema (LADAMO). *Eye (Lond).* 2023 Apr 17.

9. Wykoff CC, Abreu F, Adamis AP, Basu K, Eichenbaum DA, Haskova Z, Lin H, Loewenstein A, Mohan S, Pearce IA, Sakamoto T, Schlottmann PG, Silverman D, Sun JK, Wells JA, Willis JR, Tadayoni R; YOSEMITE and RHINE Investigators. Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. *Lancet*. 2022 Feb 19;399(10326):741-755.

If you would like to make a tax-deductible donation or discuss leaving a bequest to support macular research please visit our website sydney.edu.au/medicine/eye, 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 made out to 'The University of Sydney'

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

This newsletter is not intended to provide or substitute advice from appropriate health service providers. Although every care is taken to ensure it is free from error or inaccuracy, SSI does not make any representation or warranty regarding the currency, accuracy or completeness of this newsletter. © Copyright: 2022 Save Sight Institute. You have received this newsletter because you have, or you have shown interest in, macular disease. If you would like to receive more information, or do not wish to receive this newsletter, just let us know via email macular.news@sydney.edu.au



THE UNIVERSITY OF
SYDNEY