

Standard threshold laser versus subthreshold micropulse laser for adults with diabetic macular oedema: the DIAMONDS non-inferiority RCT

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Primary conflicts of interest: Augusto Azuara-Blanco is a member of the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Prioritisation Committee B (2020 to present). Danny McAuley is the NIHR/Medical Research Council Efficacy and Mechanism Evaluation (EME) Programme Director and member of the EME Strategy Advisory Committee, EME Funding Committee member and EME Funding Committee Remit and Competitiveness Sub-Group (2019–present). Danny McAuley is also a former member of the NIHR/UK Research and Innovation COVID-19 reviewing committee (2020–20) and the HTA General Committee (2016–18) and Commissioning Committees (2013–16). Clare Bailey has been an ad-hoc advisor for Bayer AG (Leverkusen, Germany), Novartis AG (Basel, Switzerland), Alimera Sciences (Alpharetta, GA, USA), Roche (F. Hoffmann-La Roche Ltd, Basel, Switzerland), Boehringer Ingelheim (Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany) and Janssen (Janssen Global Services, LLC, Beerse, Belgium). Victor Chong is an employee of Janssen but his role in this study is unrelated to his employment with Janssen and, thus, the content of this manuscript is not endorsed by Janssen. He has also received speaker fees from Quantel Medical (Cournon-d'Auvergne, France). Louise Downey has performed advisory board work for Bayer, Novartis, Allergan (now part of AbbVie Inc., North Chicago, IL, USA), Alimera Sciences and Alcon (Geneva, Switzerland). She has also received travel grants from Bayer, Novartis and Allergan, and research studies sponsored by Bayer, Novartis, AbbVie, Roche and Alimera Sciences. Haralabos Eleftheriadis has been an ad hoc advisor for Novartis and Bayer, received educational travel grants from Novartis, Bayer and Allergan and has given a remunerated talk for IRIDEX (IRIDEX Corporation, Mountain View, CA, USA). Faruque Ghanchi has had advisory roles for Alimera Sciences, Allergan, Apellis (Apellis Pharmaceuticals Inc., Waltham, MA, USA), Bayer, Boehringer Ingelheim, Novartis and Roche, and received travel grants from Allergan, Novartis and Roche. Robin Hamilton has received research grants from Novartis and Bayer, and received travel expenses from and attended advisory board meetings of Novartis, Bayer, Roche, Allergan and Ellex (Mawson Lakes, SA, Australia). Sobha Sivaprasad has received research grants and travel fees from and attended advisory board meetings of Novartis, Allergan, Bayer, Optos (Optos Inc. Marlborough, MA, USA), Boehringer Ingelheim, Heidelberg Engineering (Heidelberg Engineering GmbH, Heidelberg, Germany), Roche, Oxurion (Oxurion NV, Leuven, Belgium), Oculis (Oculis SA, Lausanne, Switzerland) and Biogen (Biogen Inc., Cambridge, MA, USA). Sobha Sivaprasad was a former NIHR HTA Commissioning Board member (2017–2021), Chair of the Scientific Advisory Committee of Sight UK (May 2018–present), Scientific Advisory Committee Member of Retina UK (August 2019–present), Trustee of the Macular Society (August 2019–present), as well as Chair

of the Scientific Committee of the UK Royal College of Ophthalmologists (May 2020–present). David H Steel acted as a consultant to Alcon, Gyroscope (Gyroscope Therapeutics Limited, London, UK) BVI® (Waltham, MA, USA) and Roche, and received research funding from Bayer, Alcon, Gyroscope, DORC (Dutch Ophthalmic Research Center B.V., Zuidland, the Netherlands) and Boehringer Ingelheim. James S Talks has received travel grants from Bayer and research support from Novartis. Mike Clarke is a member of the HTA Prioritisation Committee B Methods Group (2019 to present) and a former member of the HTA General Committee (2016–19). None of the authors has any commercial interest in any of the diagnostic or treatment devices used in this trial, including the lasers.

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Plain English summary

DIAMONDS non-inferiority RCT

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Plain English summary

The retina is a layer at the back of the eye. Its centre is called the macula and is responsible for central vision.

Some people with diabetes develop diabetic macular oedema. In diabetic macular oedema fluid leaks from retinal blood vessels and builds up at the macula, resulting in sight loss. Diabetic macular oedema can be mild or severe; this can be determined measuring the thickness of the macula, which is measured in micrometres (μm). One micrometre is one thousandth of a millimetre. In mild diabetic macular oedema, the thickness of the macula increases, but is less than 400 μm .

Patients with mild diabetic macular oedema can be treated with a laser and there are two laser types.

The standard threshold macular laser has been available for many years. It clears the diabetic macular oedema but produces a 'burn' in the retina.

The subthreshold micropulse laser is newer. It does not produce a burn but also clears the diabetic macular oedema. The lack of a burn, however, has led to doubts about whether or not this laser works as well as the standard threshold macular laser because 'no burn' was taken to mean 'less benefit'.

These doubts led to our establishing the DIAMONDS (DIAbetic Macular Oedema aNd Diode Subthreshold micropulse laser) trial, which compared these two lasers for people with mild diabetic macular oedema. A total of 266 people suitable for either laser joined the study at 16 NHS hospitals across the UK; 133 received standard threshold macular laser and 133 received subthreshold micropulse laser. The choice of laser was determined by chance.

The DIAMONDS trial found that the subthreshold micropulse laser was as good as the standard threshold macular laser (i.e. 'clinically equivalent') in terms of improving people's vision, reducing macula thickness, allowing people to meet driving standards and maintaining their quality of life, both in general terms and for vision in particular. There was a small increase (less than one session on average per person) in the number of laser treatment sessions needed with subthreshold micropulse laser. The costs of both laser treatments were about the same.

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